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ENVIRONMENT DIRECTORATE
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Task Force on Harmonisation of Classification and Labelling

Expert Group on Classification Criteria for Mixtures of the Task Force on Harmonisation of Classification and Labelling

REVISED DRAFT DETAILED REVIEW DOCUMENT:OVERVIEW AND COMPARISON OF EXISTING HAZARD CLASSIFICATION SYSTEMS FOR CHEMICAL MIXTURES. PART 1: MAIN DOCUMENT

4th Meeting of the OECD Expert Group on Classification Criteria for Chemical Mixtures, 28th - 29th June 1999, Dublin, Ireland, beginning on 28th June at 9.30 a.m.

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DETAILED REVIEW DOCUMENT
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I. INTRODUCTION

GENERAL

1. The success of the Globally Harmonised System (GHS) relies upon the efforts of the countries and systems involved to work together to find a consensus. Recognition is due to many who participated in this process. Acknowledgement for providing information for this detailed review document (DRD) goes to: Australia, Austria, Brazil, Canada, the European Union, IMO, Japan, Korea, New Zealand, Norway, Slovenia, Sweden, UNCETDG, and the USA. The full text of the detailed responses received is included in an annex to this document.

2. A variety of classification regulations is used in most jurisdictions to cover all the stages of a chemical's life cycle and end uses: food, drugs, cosmetics, pesticides, consumer products, radioactive materials, explosives, workplace, environmental exposure, disposal and transportation. There are important differences in the underlying philosophy and purpose of these various classification regulations. The Drafting Group collected information about all of these sectors from the respondents in order to determine what approaches are currently used, and whether the work of the Mixtures Work Group should be focused on certain sectors where harmonisation can be achieved. For the most part, all of the major existing systems other than transport have some differentiation in approach between and among these sectors.

3. Most products in commerce are mixtures. Dissimilar mixture rules and dissimilar hazard classifications can currently result in different conclusion about the same commercial product. The harmonisation of criteria and methodology for the classification of mixtures is at the heart of the Globally Harmonised System (GHS).

4. It should be noted, however, that while there is an underlying concern about the outcome of the differing mixture rules in terms of inconsistent hazard communication, the purpose of this activity is to focus on the criteria and methodology for classification. Work concerning the warnings that will be placed on labels for mixtures, or information on material safety data sheets, is to be performed by the Hazard Communication Work Group being convened by the International Labour Organisation (ILO).

5. This Step 1 Detailed Review Document (DRD) will focus on the health and environmental hazards of mixtures. The physical hazards of mixtures are being dealt with by the ILO/UN-CETDG Focal Point. The final proposal for a harmonised system for the classification of mixtures will include the physical, the health and environmental hazards. In cases where existing systems have environmental criteria for mixtures they are included for information in an annex.

APPROACHES TO COVERING MIXTURES

6. An examination of the major existing systems indicates that the approaches to regulating mixtures can be grouped into categories based on available test data:

a) tested mixtures;
b) "bridging data" or partially tested mixtures; and
c) untested mixtures.

7. Tested mixtures are generally treated and classified in all classification systems the same way that substances are treated and classified. However, in the EU system, testing cannot be used to assess the carcinogenic, mutagenic and reproductive hazards of mixtures. In all systems whenever relevant evidence of effects on man is available on mixtures, this information generally takes precedence in classification.

8. Some systems rely upon *bridging data*/extrapolation to evaluate the effects of mixtures where there are no or incomplete data. For some mixtures, sufficient data are available for constituent ingredients to allow reliable extrapolation of the hazard of the mixture. It must be demonstrated that the new ingredient would not alter the toxicological profile for the formulation. For example, in a tested mixture one ingredient can be replaced by an analogue of similar toxicity either based on testing or SAR data. Pesticide regulations in the USA and Canada accept bridging data, particularly for acute hazards.

9. The term "untested mixtures means the mixture as a whole has not been tested. There may be data available for some/all of its constituents. Some systems cover *untested mixtures* through application of a standardised approach. These approaches are intended to ensure that all mixtures are evaluated in some fashion based on the available information, and that these evaluations are comparable for all untested mixtures under that system. It appeared to the Working Group in Ottawa that this is the area where harmonisation is most likely to be achievable. Thus standardised approaches to classification of untested mixtures are the main focus of the DRD.

10. There are several standardised approaches to the classification of untested mixtures in the existing systems. In general the workplace systems in USA and Canada use a percentage cut-off approach, i.e., the mixture is classified according to the hazards of the ingredients that are present at levels above specified percentages. The European system uses a similar concentration limit of ingredients approach to classification and applies it to preparations both in the workplace and in the consumer use setting. For certain endpoints in the EU system additivity of effects are taken into consideration and formulas are applied for this purpose. The UN transport system uses a general approach based on human experience or testing, when data are available; for some end-points, formula based on concentrations are used; in a few cases, concentrations are sued; in a few cases, concentration limits are provided for specific mixtures. All of the other sectors use either test data or bridging data in the existing systems (e.g., pesticides), or focuses on listing ingredients on product labels rather than hazard classification and labelling (e.g., cosmetics). There is further discussion of each of the sectors below to address the appropriateness of including them in the harmonisation effort.

CHEMICAL COMPOSITION

11. In the existing systems the standardised approaches to the classification of untested mixtures all rely on knowing the chemical composition down to either a percentage cut-off or a concentration limit.

PHYSICAL STATE

12. In the EU system, the percentage cut-off or concentration limits for the components of the mixture differ according to the physical state.

II. DEFINITIONS

GENERAL

13. An examination of the existing systems reveals a lack of harmonisation in terminology in a number of respects. Some specific definitions are examined in this report, and it is expected that the Step 2 document will propose harmonised definitions in these areas. However, for purposes of establishing a common understanding of the systems covered in this report, it may be helpful to review some of the areas where different terms are used, but the concept is actually the same.

14. The DRD uses the term “mixtures” to describe the coverage of the work. This is the term used in North American systems for the workplace, but it appears to be identical to the term “preparations” used in Europe. Similarly, in other parts of each country’s regulatory approach to the subject, there may be other terms used such as “products” or “formulations”. For purposes of this document, these terms are also considered to be synonymous to “mixtures” or “preparations”.

15. In the UN transport system, the word “substance” is used to cover both the terms “substance” and “mixture”. The terms “formulation” and “preparation are also sometimes used.. Other variations are found in the terms used to describe the process through which the hazards of a mixture are ascertained. In the EU, this process is referred to as “hazard classification.” In the US HCS, the term is “hazard determination” or “hazard evaluation”. Another term in use is “hazard identification”. It appears that these terms are synonymous in most cases as well, and refer to the identification of relevant data regarding the hazards of a chemical or substance, and the subsequent review of that data to ascertain what hazards may be associated with it.

16. The one exception to the generally consistent approach to interpretation of these process- related terms involves consumer products in the US. Under that system, “classification” embodies a two- step process of identifying the hazard and performing an assessment of the likelihood of harm or injury for purposes of labelling. Classification under CPSC involves determination of likelihood of injury or illness, the extent of which may vary from gross/blanket determination (e.g. use of dose related cut off points for acute toxicity since a single exposure is sufficient to injure) to a detailed risk determination as appropriate. The DRD only addresses the first step of this process, i.e., identification of the hazard. It must therefore be recognised that the term “classification” when used in conjunction with the US consumer products regulations has a broader meaning than what is envisioned in this report. The report uses the terminology in the sense that it appears it is used in the majority of the systems addressed as the first step in the process or identification of the hazard. The second step - deciding what is appropriately conveyed about the chemical on the label - will be addressed in a separate forum and is not within the purview of this Work Group.

17. Another area where different terminology is used to address a similar concept is in the standardised or conventional approaches. The EU system refers to “concentration limits” for different endpoints, while the North American systems for workplace use the term “percentage cut-offs” to describe their approach. These appear to mean the same thing, although the numbers used may vary somewhat.

18. Definitions of pertinent terms (chemical/substance, mixture/preparation) from various existing classification systems are given by end use in the Appendix I tables. The tables in Appendix I include the source of the definitions, i.e., legislation, regulation, etc.

OTHER DEFINITIONS

Definitions According to the Canadian Legislation

The Workplace Hazardous Materials Information System (WHMIS)

19. "*Controlled Product*" means any product, material, or substance that meets any of the following criteria listed in Part IV of the *Controlled Products Regulations*: (A) compressed gas; (B) flammable and combustible material; (C) oxidising material; (D) poisonous and infectious material; (E) corrosive material and (F) dangerously reactive material.

20. "*Manufactured Article*" means any article that is formed to a specific shape or design during manufacture, the intended use of which when in that form is dependent in whole or in part on its shape or design, and that under normal conditions of use, will not release or otherwise cause a person to be exposed to a controlled product.

21. "*Complex Mixture*" means a mixture that is a combination of many chemicals, has a commonly known generic name and is:

a) naturally occurring;
b) a fraction of a naturally-occurring mixture that results from a separation process; or
c) a modification of a naturally-occurring mixture or a modification of a fraction of a naturally-occurring mixture that results from a chemical modification process.

Consumer products

22. "*Consumer Chemical Product"* means a chemical product that is destined for use by a consumer set out in item 1 of Part II of Schedule I to the *Hazardous Products Act* and has the properties set out in one or more of (a) Category 1, toxic products, in Part 1; (b) Category 2, corrosive products, in Part 2; (c) Category 3, flammable products, in Part 3; and (d) Category 4, quick skin-bonding adhesives, in Part 4.

23. There is no definition of article, however, for consumer products, the criteria apply only to components or generated products to which the user or others might become exposed in normal use or reasonably foreseeable use. The Regulations do not apply to a consumer chemical product if a user cannot be exposed to the product or to any of its hazardous ingredients during normal use or reasonably foreseeable use.

24. The terms "hazard identification", "hazard evaluation", "hazard determination", "hazard classification", and similar terms for purposes of comparing the various approaches are not defined in the regulation.

Pesticides

25. The Canadian *Pest Control Products Act* defines a control product as "any product, device organism, substance or thing that is manufactured, represented, sold or used as a means for directly or indirectly controlling, preventing, destroying, mitigating, attracting or repelling any pest and includes

a) any compound or substance that enhances or modifies or is intended to enhance or modify the physical or chemical characteristics of a control product to which it is added, and

b) any active ingredient used for the manufacture of a control product.

Definitions According to the European Legislation

26. Directives 67/548/EEC on dangerous substances and 88/379/EEC on dangerous preparations contain definitions for placing on the market of substances and preparations.

27. "*Placing on the market*" means the making available to third parties. Importation into the Community customs territory shall be deemed to be placing on the market for the purposes of the Directives.

28. "*Substances*" mean chemical elements and their compounds in the natural state or obtained by any production process, including any additive necessary to preserve the stability of the products and any impurity deriving from the process used, but excluding any solvent which may be separated with out affecting the stability of the substance or changing its composition. A substance may be chemically very well defined (e.g. acetone) or a complex mixture of constituents of variable composition (e.g. aromatic distillates). For some complex substances, some individual constituents have been identified.

29. "*Preparations*" mean mixtures or solutions composed of two or more substances.

30. "*Chemical agent*[1]*"* means any chemical element or compound, on its own or admixed, as it occurs in the natural state or as produced, used or released, including release of waste, by any work activity, whether or not produced intentionally and whether or not placed on the market.

31. "Hazardous chemical agent[1]" means:

1) Any chemical agent which meets the criteria for classification as a dangerous substance according to the criteria in Annex VI to Directive 67/548/EEC, whether or not that substance is classified under that Directive, other than those substances which only meet the criteria for classification as dangerous for the environment;
2) Any chemical agent which meets the criteria for classification as a dangerous preparation within the meaning of Directive 88/379/EEC, whether or not that preparation is classified under that Directive, other than those preparations which only meet the criteria for classification as dangerous for the environment;
3) Any chemical agent, which, whilst not meeting the criteria for classification as dangerous in accordance with (1) and (2), may, because of its physico-chemical, chemical or toxicological properties and the way it is used or is present in the workplace, present a risk to the safety and health of workers, including any chemical agent assigned an occupational exposure limit value.

32. "*Article*" is defined as: an item which is formed to a specific shape, surface or design during manufacture, has end use function(s) dependent in whole or in part upon its shape or design during end use, and has either no change of chemical composition during its end use or only those changes of composition which have no commercial purpose separate from that of the article.

1 Definitions from Directive 98/24/EEC (OJ No L 131, 5.5.1998, p. 11)

Note: The definition of an article is not included in the Directives on dangerous substances or dangerous preparations. Definition for an article is, however, specified in the document "Reporting for the EINECS Inventory".[2] This document was introduced as a guidance by Commission Decision 81/437/EEC[3] on laying down the criteria in accordance with which information relating to the inventory of chemical substances is supplied by the Member States to the Commission.

33. "Hazard identification" is the identification of the adverse effects which a substance has an inherent capacity to cause.

Note: Hazard identification" is defined in Commission Regulation 1488/94[4] and Commission Directive 93/67/EEC[5] This definition of hazard identification does not contain the element of determination of the classification on the basis of the data on adverse effects and the classification criteria. Hazard identification can be considered as a first step for classification.

Definitions According to US Legislation

US OSHA:

34. Under the Hazard Communication Standard: "Workplace" means an establishment, job site, or project, at one geographical location containing one or more work areas. "Work area" means a room or defined space in a workplace where hazardous chemicals are produced or used, and where employees are present.

US CPSC:

35. The Consumer Product Safety Act defines consumer product as any article, or component thereof, produced or distributed (i) for sale to a consumer for use in or around a permanent or temporary household or residence, a school, in recreation or otherwise, or (ii) for the personal use, consumption or enjoyment of a consumer in or around a permanent or temporary household or residence, a school, in recreation or otherwise; but does not include foods, drugs, cosmetics, pesticides, tobacco and tobacco products, motor vehicles and motor vehicle equipment, fire arms and ammunition, aircraft and its parts and appliances, and boats that are subject to Federal Boat Safety Act.

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2 European Commission, Constructing EINECS: Basic documents, Reporting for the EINECS In ventory, Office for Official Publications of the European Communities, L-2985 Luxembourg, ISBN 92-825-2459-0.

3 OJ No L 167, 24.6.1981, p.31.

4 Commission Regulation No 1488/94 laying down the principles for the assessment of risks to man and the environ ment of existing substances in accordance with Council Regulation No 793/93, OJ No L 161, 29.6.1994, p.3.

5 Commission Directive 93/67/EEC laying down the principles for assessment of risks to man and the environment of substances notified in accordance with Council Directive 67/548/EEC, OJ No L 227, 8.9.1993, p. 9.

III. SCOPE

CANADA

36. The *Hazardous Products Act* covers consumer (Part I) and workplace (Part II) chemicals, with certain exemptions. Chemicals used in the workplace are covered by the Controlled Products Regulations and the system is based on hazard classification and communication. The Workplace Hazardous Materials Information System (WHMIS) establishes uniform national requirements to ensure that information regarding health hazards, safe use, storage and handling of hazardous materials are disclosed on the MSDS. Information on toxicological properties should be provided without limiting such information to the hazards based on presumed use. WHMIS does not necessarily take into account the possibility of exposure. Information that is applicable to the product should be reported. There are no special considerations for susceptible populations in WHMIS.

37. WHMIS Exclusions: At present, the WHMIS requirements of the *Hazardous Products Act* do not apply to the following categories of products:

1. Product, material or substance packaged as a consumer product
2. Explosives
3. Cosmetic, drug, food, or device within the meaning of the Food and Drug Act
4. A pest control product within the meaning of the Pest Control Products Act
5. Radioactive materials
6. Hazardous waste
7. Wood or product made of wood
8. Manufactured articles
9. Tobacco or products made of tobacco

Note: The products excluded from WHMIS are currently under review. Tripartite sectoral committees have reached consensus agreement that explosives, cosmetics, drugs, foods, devices, pest control products, radioactive substances, hazardous waste and consumer products (Items 1 to 6) would be covered by WHMIS.

38. Consumers products are covered by Consumer Chemicals and Containers Regulations of the Hazardous Products Act. Only acute hazards are covered at this time. No environmental endpoints are covered in the Hazardous Product Act. The system applies for exposure during normal use or reasonably foreseeable use. Children are a target population in developing criteria for consumer products, as they may be more sensitive to toxic chemicals than adults, are more likely to use products inappropriately (especially with regard to ingestion), are unable to understand labels and are less able to protect themselves if exposed.

39. Consumer Product Exclusions: Components which cannot be made accessible to the user or others, by virtue of the product form or formulation, will not be subject to the criteria.

40. All pesticides are covered under the ***Pest Control Products Act***.

EUROPEAN UNION

41. The EU Directives on the classification, packaging and labelling of Dangerous Substance and Dangerous Preparations cover chemicals intended for both consumer and workplace use. The EU directive on Dangerous Substances and the proposal for a new Directive on Dangerous Preparations include the

classification "dangerous to the environment" which the CPSC, the Canadian consumer chemical regulations, WHMIS and OSHA do not.

Existing Directive

42. The EU Directive 88/379 covers classification, packaging and labelling of dangerous preparations when they are placed on the market in the EU Member States. The Directive is applied to preparations which contain at least one substance classified as dangerous and which are considered to be dangerous within the meaning of the Directive. The aim is to protect both professional users and general consumers as well as the environment.

43. Some groups of preparations are exempted from the Directive; in these cases there are other specific Directives for protection of health and safety and in some cases the environment when the product is placed on the market. Preparations are excluded when intended to the final user or consumer. In cases where raw materials or intermediates to any of the exempted groups, i.e. preparations not intended for the final user, are placed on the market they are covered by the Directive.

44. The exempted groups of preparations are:

- medical and veterinary products
- cosmetic products
- mixtures of substances which in the form of waste are covered by specific legislation
- pesticides
- munitions and explosives
- foodstuffs and animal feeding stuffs in a finished stage intended for the final consumer.

45. In addition the Directive does not apply to the carriage of dangerous preparations by rail, road, inland waterway, sea or air or to preparations in transit which are under customs supervision provided they do not undergo any treatment or processing.

46. In the proposed new Directive the following changes of the scope have been proposed:

- pesticides, munitions and explosives (if in the form of chemical) shall be within the scope
- preparations containing radioactive substances shall be excluded
- those medical devices which are invasive or used in direct physical contact with the human body shall be excluded insofar as other specific legislation gives the same level of information provisions and protection.

47. In addition some provisions of the Directive shall apply to preparations which are *not* classified as dangerous but might nevertheless present a specific hazard.

Proposal for New Directive on Dangerous Preparations

48. Proposal (COM(96)347,[6] COM(97)462[7]) for the new Directive of the European Parliament and the Council on the classification, packaging and labelling of dangerous preparations is in the decision making process of the EU institutions.

49. The proposal contains the following new elements:

- Classification & labelling of preparations dangerous for the environment. (The classification principles for preparations dangerous for the environment are similar to the conventional method applied to classification for [acute lethal] health hazards. The preparations are classified as dangerous for the environment on the basis of component substances and their concentrations in the mixture);

- Classification, packaging, labelling and Safety Data Sheet requirements for pesticides (plant protection products and biocides);

- Classification of explosives;

- Extends certain specific provisions to preparations which are not classified as dangerous;

- Consolidates and updates existing EU legislation and rationalises the structure of the Directive. Consequently the key principles are in the main text. The technical detail is contained in the annexes which can be more quickly amended to take account of technical developments. A recognition that the characteristics of alloys are such that it may not be possible accurately to determine their properties using currently available conventional methods. It is therefore necessary to develop a specific method of classification which takes into account their particular chemical properties.

UNCETDG:

50. The UN Recommendations on the Transport of Dangerous Goods (UNRTDG) are not regulations in themselves, but are formatted as a model intended for adoption in international transport modal regulations and for national transport regulations, but they have also been used in some countries as a basis for supply legislation. The UNRTDG prescribe detailed requirements applicable to the transport of dangerous goods and cover all products whatever their end use is intended to be; wastes are also covered. The UNRTDG do not apply to the transport of dangerous good in bulk, dangerous goods required for the propulsion of the means of transport or for the operation of its specialised equipment, dangerous goods, packaged for retails sale carried by individuals for their own use.

US:

51. The OSHA Hazard Communication Standard covers chemicals in the workplace. Consumer products and cosmetics in commerce and pesticides are covered by separate regulations. No environmental end points are covered.

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6 OJ C283, 26.9.1996, p. 1.

7 OJ C.

US CPSC:

52. The classification and resultant labelling for consumer products (FHSA) is based on the determination of likelihood of injury or illness. Thus products not likely to cause injury or illness when used or foreseeably misused are not classified or labelled. The following exemptions are based on similar principle:

> Common matches, including book matches, wooden matches, and so-called "safety" matches; paper items such as newspapers, wrapping papers, toilet and cleansing tissues, and paper writing supplies; thread, string, twine, rope, cord, and similar materials; laboratory chemicals intended only for research or investigation and other laboratory uses (except those in home chemistry sets); rigid or semi-rigid ballpoint ink cartridges; the ink does not have an LD_{50} single oral dose of less than 500 milligrams per kilogram of body weight of the test animal, and the cartridge does not have a capacity of more than 2 grams of ink; porous-tip ink-marking devices; glues with a cyanoacrylate base in packages containing 3 grams or less; liquid fuels containing more than 4 percent by weight of methyl alcohol that are intended and used for operation of miniature engines for model aeroplanes, boats, cars, etc.; solid fuel pellets intended for use in miniature jet engines for propelling model jet aeroplanes, speed boats, racing cars, and similar models, kits intended for construction of model rockets and jet propelled model aeroplanes requiring the use of difluorodichloromethane as a propellant. It should be noted that these exemptions require products to meet specific conditions and may require specific labelling.

US OSHA:

53. The Hazard Communication Standard has a complicated set of exemptions that relate primarily to the standard's interface with other US laws and regulations, or to situations where exposure is so minimal that the risk is expected to be very small. The only ones that will be addressed here are those that deal with application to a specific product, rather than application in a type of workplace (such as a laboratory). It is unlikely that these exemptions would have broad enough application to be part of the GHS approach. It should be noted that these exemptions do not solely apply to mixtures; substances would also be subject to the same exemptions.

54. Additional labelling under the HCS is not required for products subject to other Federal labelling laws as follows (other requirements of the standard for MSDSs and training may be applied):

- Pesticides labelled in accordance with EPA requirements
- Chemical substances labelled in accordance with EPA requirements under the Toxic Substances Control Act
- Food, food additives, colour additives, cosmetics, or medical/veterinary devices or products, when regulated by FDA or the Department of Health
- Alcoholic beverages regulated by the Bureau of Alcohol, Tobacco and Firearms
- Consumer products or hazardous substances regulated by CPSC
- Agricultural or vegetable seed regulated by the Department of Agriculture

55. The following are totally exempted from the HCS:

- Hazardous waste when regulated by EPA
- Tobacco or tobacco products
- Wood or wood products (treatment chemicals are covered, as is wood dust that can be inhaled).
- Articles (an "article" is defined as follows: a manufactured item other than a fluid or particle: (i) which is formed to a specific shape or design during manufacture; (ii) which has end use function(s) dependent in whole or in part upon its shape or design during end use; and (iii) which under normal conditions of use does not release more than very small quantities, e.g., minute or trace amounts of a hazardous chemical (as determined by paragraph (d) of this section), and does not pose a physical hazard or a health risk to employees)
- Food or alcoholic beverages which are sold, used or prepared in a retail establishment, or food intended for personal consumption by employees while in the workplace
- Drugs that are in solid, final form for direct administration to a patient; packaged for sale to consumers in a retail establishment; and intended for personal consumption of employees while in the workplace
- Cosmetics which are packaged for sale in a retail establishment, or in the workplace for the personal consumption of employees
- Consumer products which are used in the workplace for the purpose intended by the manufacturer, and the use results in a duration and frequency of exposure which is not greater than the range of exposures that could reasonably be experienced by consumers
- Nuisance particulates
- Ionising and non-ionising radiation
- Biological hazards

US EPA:

56. Under FIFRA section 25(b) the following exclusions from the requirements of registration have been set forth:

- pheromones used only in traps and pheromone traps
- treated articles such as wood treated with preservatives
- embalming fluids
- horticultural products consisting of plant hormones, plant nutrients, inoculants, or soil amendments not intended for use on food crops and of low toxicity
- natural cedar

- foods containing no active ingredients and used to attract pests
- certain minimum risk pesticides such as castor oil, soybean oil, rosemary, sesame, etc.

IV. RATIONALE FOR EACH APPROACH

57. There are some important differences in the underlying philosophy and purpose of the existing classification systems.

BASIS FOR EXISTING SYSTEMS

58. The primary objective of chemical classification and labelling systems is to enhance protection of human health and the environment. The key principle in the USA and Canadian systems is to convey health and environmental effect information on chemicals to the user in a manner that will most appropriately meet the user's needs. They vary in where and how they provide the information and the level of detail based on knowledge of potential exposures.

59. The presence of chemicals in all economic sectors has resulted at the national level in the elaboration of sector-specific health and environmental regulations which are targeted to the chemical users in each sector (transport, workplace, agriculture, consumer products). Specific regulations are designed to protect specific populations and are based on knowledge of uses and exposures and how health effects information can be can be transmitted to those populations. Sector-specific regulations are necessitated by 1) differences in the knowledge of specific exposures available to a chemical's producer which, because of differences in the degree of uncertainty that this causes, limits to varying degrees the safety information communicated by the chemical manufacturer, and 2) the need to organise complex health and environmental knowledge in such a way that appropriate information is conveyed in a form that is easily understood and applied by chemical users, while taking into account the presence or absence of other tools (e.g., MSDSs, training). The key principle in the EU system is that hazard classification provides the foundation for a wide range of harmonised legislative processes which allow effective risk management and covering the whole life cycle of substances and preparations. The legislation facilitates the free movement of goods whilst ensuring a high level of protection of human health and the environment.

CANADA: WHMIS

60. The Workplace Hazardous Materials Information System (WHMIS) is a national information system designed to protect Canadian workers by providing safety and health information about hazardous workplace materials. WHMIS was developed through a consensus process with representation from industry, organised labour, and federal, provincial and territorial governments. WHMIS recognises the interests of workers, employers, suppliers and regulators and balances the workers right to know with industry's right to protect confidential business information.

61. The WHMIS classification system is based on cut-offs which presumes that a mixture is hazardous if it contains a hazardous ingredient at a concentration exceeding a specified cut-off. The use of cut-offs is administratively straightforward and can be applied by using available data on the toxicology of ingredients in the mixture. Since WHMIS is primarily an information system, the use of cut-off values is justifiable as a means of consistently communicating information about hazardous ingredients, as contrasted with providing a hazard evaluation of the mixture. The numerical values of cut-offs, however, are necessarily arbitrary and were chosen largely for consistency between Canada and the United States.

62. The classification of substances and mixtures is the responsibility of the supplier (or employer). There is no regulatory agency involved in classification. Hazard categorisation (i.e., sub-classifying the overall hazard classification into severity levels) is used in the Canadian system for selecting hazard symbols for hazard communication. The hazard communication audience is the worker/customer. The focus is on hazard identification and its subsequent communication.

63. The *Consumer Chemicals and Containers Regulations* are intended to ensure that consumers have ready access to the required knowledge. This is accomplished by requiring precautionary labelling to appear on containers of hazardous chemical products intended for domestic use. The labelling provides warnings about the dangers involved with the use, handling and storage of the products, the steps to take in case of an accident and recommendations for first aid treatments. Child-resistant packaging is also prescribed for some products. The *Consumer Chemicals and Containers Regulations* are intended to reduce the injuries and costs caused by accidents involving consumer chemical products.

EU

64. The philosophy of the European Union requires harmonised legislation that facilitates the free movement of goods whilst ensuring a high level of protection of human health and the environment The EU standardised approach allows that all hazard end points can be specified easily, reliably and inexpensively without animal testing.

65. The EU system for hazard classification provides the foundation for a wide range of legislative processes covering the whole life cycle of substances and preparations including e.g. hazard communication, risk assessment, worker protection, protection of the environment, prevention of major accidents and restrictions for marketing and use. Hazard classifications are scientifically defensible and robust and reflect in a credible way the real hazards of preparations.

66. Because of a number of legislative consequences it is important that the hazard classifications are scientifically defensible and robust and reflect in a credible way the real hazards of preparations.

67. Hazard classification is the responsibility of the manufacturer, importer or distributor. Classification of a mixture is based on classification of substances. The classification for a substance in Annex I to Directive 67/548/EEC has to be used, if available. If the substance is not listed in this Annex the manufacturer or importer shall classify the substance. On the basis of the classification(s) of substances the preparation is classified by applying the concentration limits for different end points.

68. Labelling and Safety Data Sheets (SDS) for professional users are consequences of classification. The information on classification is passed to the users of chemicals by the supply chain to make sure that the users are aware of the hazards so that employers or economic operators can take appropriate measures for protection of workers and the environment. The obligations set by other Community legislation may be triggered by the classification of the preparation.

69. Safety Data Sheets (SDS) submit information on dangerous components of classified preparations to the professional users. Information shall be given on components classified as dangerous to health and/or to the environment, and present at levels of 1% or greater (unless the classification limit is lower than 1%). The employer or economic operator should use this information for risk assessment purposes. This information may be needed e.g. in cases where several preparations containing similar substances are used simultaneously, or in cases where large amounts of preparations containing low concentrations of dangerous substances are used and total emissions to the environment could be significant. On the basis of the risk assessment carried out by the employer or economic operator appropriate steps should be taken for protection of health of workers and the environment.

70. An obligation to submit information by SDS also on non-classified preparations will be introduced by the new Directive on dangerous preparation. This obligation would apply to preparations that contain 1 % or more of a substance dangerous to health or to the environment, or of a substance for which a Community Exposure Limit in the work place has been defined.

71. The workers have access to the information of SDSs. The label information is available to anyone.

UNCETDG

72. The UNRTDG have been developed in light of technical progress, the advent of new substances and materials, the exigencies of modern transport systems and, above all, the requirement to ensure the safety of people, property and the environment.

73. The UNRTDG includes a Dangerous Goods List which lists the dangerous goods most commonly carried together with their hazard classes (primary and subsidiary risk). Classifications have been made on the basis of consideration of data submitted to the UNCETDG by governments, intergovernmental organisations and other international organisations. However, the actual data submitted are not formally endorsed by UNCETDG. Classification for dangerous goods, not listed in the above mentioned lest, is made by the consignor unless it is specifically required that the classification shall be made by the competent authority.

US: OSHA HCS

74. The OSHA Hazard Communication Standard provides exposed workers and employers using a chemical in their workplaces with the right to know the identities and hazards of those chemicals. The underlying philosophy is that the availability of information allows the selection and use of appropriate control measures, thus resulting in fewer illnesses and injuries based on chemical exposures. It thus is based on the premise that as complete disclosure as possible is the best approach. This desire for disclosure was balanced by concerns about trade secret claims (which are more common for chemicals in small concentrations) and the need for information about very small quantities. The percentage cut-offs were selected as a practical and pragmatic approach to addressing these concerns, while still ensuring that necessary information is readily available to employers and employees.

75. OSHA uses the term hazard determination for evaluation of the hazards. While appropriate hazard information must be provided, it is not required to name, assign, or cite a hazard category or hazard class under the OSHA HCS. No regulatory agency is involved in classification. The appropriateness of the classification may be assessed by the Agency's enforcement personnel. The hazard communication audience is the worker/customer. The focus is on hazard identification and its subsequent communication. As has already been indicated in the description in the annex, the cut-off values were based on the need for protection, ease of application, and reasonableness of approach. It did not appear to OSHA at the time this rule was promulgated that there is any specific science that indicates an appropriate cut-off for any particular endpoint. It is a policy determination rather than a scientific one.

US: FHSA

76. U.S. regulations applicable to consumer products are based on the *Federal Hazardous Substances Act* (FHSA), which covers most consumer products, with exception of some specific types of consumer products, such as pharmaceuticals and cosmetics. Due to a difference in objective, consumer product labelling regulations are based on principles that are different from workplace systems such as the Hazard Communication Standard. The purpose of U.S. consumer product regulations is to protect the public from unreasonable risk associated with consumer products by communicating the likelihood of injury that could occur as a result of use and reasonable foreseeable misuse. Therefore, the U.S. regulations under FHSA incorporate critical elements in classification that allow determination of the likelihood of injury based on available exposure data. Since there are no formal mechanisms for training

consumers or distributing MSDSs to them, the consumer product manufacturer must assume the combined role of the chemical supplier who develops information on hazards for MSDSs and labels, and the employers who are to utilise information on exposures to evaluate risk to support training. The additional information taken into account provides greater differentiation among hazards, thereby capturing the consumer attention to hazards that are likely to cause injury if not managed. This improves prospects that consumers will take appropriate precautions in handling materials.

V. DESCRIPTION OF EXISTING SYSTEMS

77. Appendix II of the DRD contains tables which compare the existing systems by end use: workplace, pesticides, consumer and cosmetics. In the European system the workplace and consumer products have similar requirements. In New Zealand the systems for the workplace, pesticides and consumer products are similar for chemicals used professionally and for consumers. See Appendix II Table IV-3 for a comparison of workplace systems, Table IV-4 for pesticides, Table IV-5 for consumer products and Table IV-6 for cosmetics.

78. This section also gives a detailed description of the workplace systems which include the standardised approach to untested mixtures, the role of test data and the role of national requirements compared to state, province and territory requirements. Table IV-2 compares the health endpoint cut-off values for the major workplace and transport systems. The major workplace systems, as well as the systems responding to the questionnaire other than the CPSC, all use concentration cut-offs as part of the standardised approach to mixture classification.

79. Under the OSHA HCS the chemical manufacturer, importer or employer is responsible for determining the hazard of the mixture. The appropriateness of the classification may be assessed by the Agency's enforcement personnel. In WHMIS the responsibility for the classification of the mixture rests with the Canadian supplier, distributor or importing agent. In the EU when preparations are placed on the market of the Member States, the manufacturer, or those responsible for placing on the market (importer, distributor or any other person) shall comply with the requirements of the Directive. The employer has the obligation to identify the hazards and risks in the work place.

WORKPLACE

Canada: The Workplace Hazardous Materials Information System (WHMIS)

Standardised approach

80. Workplace Hazardous Material Information System (WHMIS) of the *Controlled Products Regulations*: Controlled products that are untested mixtures with respect to one or more applicable toxicological endpoints specified in the CPR must be evaluated on the basis of the hazards associated with each ingredient present at a reportable concentration in the mixture. In the case of a controlled product that is an untested mixture, the mixture is generally considered to have the same toxicological hazards as the ingredients subject to disclosure present at or above the cut-off concentrations. WHMIS requires the disclosure of the chemical identity and the concentration of any ingredient of which toxicological properties are not known to the supplier. Information on toxicological properties should be provided without limiting such information to the hazards based on presumed use or exposure. There are no special considerations for mixtures based on physical state in WHMIS. Information that is applicable to the product should be reported. There are no special considerations in WHMIS for mixtures that separate. There are no special considerations for impurities/contaminants. Impurities/contaminants will be treated as hazardous ingredients if they meet WHMIS criteria. The Material Safety Data Sheet (MSDS) must list any substances, materials or products which interact with the controlled product to produce a toxic effect greater than the sum of their separate effects, if this information is available. There are no criteria/rules in WHMIS when concentrations of initial ingredients are changed or when new components that have very similar or the same properties are substituted.

81. Percentage: Reportable concentrations are 0.1% w/w or more for substances which meet the classification criteria for teratogenicity, embryotoxicity, carcinogenicity, reproductive toxicity, germ cell mutagenicity, or respiratory tract sensitisation. The concentration cut-off is 1% w/w for all other

toxicological criteria in WHMIS (i.e., acute and chronic toxicity, somatic cell mutagenicity, skin and eye irritation, skin corrosion and dermal sensitisation).

82. Acute toxicity LD_{50}/LC_{50} values: Where the LD_{50} or LC_{50} of one or more ingredients of a mixture is not known, the LD_{50} or LC_{50} of the mixture is equal to the most acutely lethal ingredient that is present in the mixture at a concentration of one percent or more.

Addition rule: If LD_{50}/LC_{50} values are known for each ingredient present in the mixture at 1% w/w, the product LD_{50}/LC_{50} may be calculated using the following formulas

for a solid or a liquid:

$$\frac{1}{LD_{50} \text{ of mixture}} = \frac{\text{Proportion of Ingredient A}}{LD_{50} \text{ of Ingredient A}} + \frac{\text{Proportion of Ingredient B}}{LD_{50} \text{ of Ingredient B}} + \frac{\text{Proportion of last Ingredient}}{LD_{50} \text{ of last Ingredient}}$$

for a gas, vapour, dust, mist or fume:

$$\frac{1}{LC_{50} \text{ of mixture}} = \frac{\text{Proportion of Ingredient A}}{LC_{50} \text{ of Ingredient A}} + \frac{\text{Proportion of Ingredient B}}{LC_{50} \text{ of Ingredient B}} + \frac{\text{Proportion of last Ingredient}}{LC_{50} \text{ of last Ingredient}}$$

Role of test data:

83. Tested Mixtures: Test data, when available, are the basis for classification of mixtures. If products have been tested, it is these data that are used for classification and MSDS disclosure.

84. Section 33(1) of the *Controlled Products Regulations* (CPR) states that for the purpose of establishing that a product in included in one of the six WHMIS classes, a supplier shall use: results from testing; or evaluation and scientific judgement based on tests results with respect to the product or where appropriate, a product that has similar properties. The supplier may also use information of which he is aware or ought reasonably to be aware in place of those criteria listed above.

85. The extent to which professional judgement is used by a supplier will depend on the specific criteria being considered. The WHMIS Information Bulletin No. 8 provides guidance on the use of professional judgement in the classification of controlled products under WHMIS.

86. Neither the *Hazardous Products Act* (HPA) nor the CPR impose a requirement for the testing of materials in order to classify them for any of the WHMIS classes. If a supplier (or employer, manufacturer or importer) decides to test a mixture, data would not have to be submitted to a governmental agency for review. Therefore, it is impossible to determine if testing relates to ingredients or mixtures.

> Note: However, there is one exception. In some instances an employer, supplier, importer or manufacturer may not wish to disclose the identity or concentration of an ingredient in a controlled product. In this case, a trade secret claim may be filled with the Hazardous Materials Information Commission (HMIRC) for exemption from the full requirements of WHMIS. All toxicological data that were used to prepare the MSDS would have to be submitted to the HMIRC for review. Most of the WHMIS controlled products reviewed for trade secrets are untested mixtures with respect to toxicological properties.

87. Incomplete Data Set: When complete test data is not available on the mixture itself, one may also use human data, professional judgement and test results with a product, material or substance that has similar properties.

88. Bridging Data/Extrapolation: When all end points are not tested, ingredient data are used for toxicity end points that were not tested. Professional judgement may also be used. There are no bridging rules or criteria for extrapolation of data in the workplace legislation. On the other hand, there are no provisions per se in WHMIS that would prevent the use this approach.

> Note: It is the supplier who has the legal responsibility to determine if a product meets WHMIS criteria. Therefore, as specified in CPR Section 33(2), "...the supplier may use information of which the supplier is aware or ought reasonably to be aware..." for classification. WHMIS Information Bulletin No. 12 states: Any toxicological information resulting from tests on a mixture must be disclosed if available and applicable to the mixture. Information relating to ingredients subject to disclosure must be disclosed if this information is applicable to the mixture.

Role of federal legislation

89. The federal legislation requires suppliers of hazardous workplace materials to label containers and provide MSDS as a condition of sale and importation. Since the provinces and territories have constitutional responsibility over matters relating to occupational safety and health (OSH) and Human Resources Development Canada (HRDC) is responsible for OSH matters in federally-regulated work sites, complementary and interlocking WHMIS legislation in each of these jurisdictions requires employers to classify material used in the workplace, to provide labels, MSDSs and worker education and training programs.

European Union: Dangerous Preparations Directive

Standardised approach

90. The object of classification is to identify all the toxicological, physico-chemical and ecotoxicological properties of substances and of preparations which may constitute a risk during normal handling or use.

91. Classification of substances is based on their intrinsic properties according to the categories of danger (very toxic, toxic, harmful, corrosive, irritant, sensitizing, carcinogenic, mutagenic, toxic to reproduction, explosive, oxidising, extremely flammable, highly flammable, flammable, dangerous for the environment). The general principles of classification of substances and preparations shall be applied according to the criteria in Annex VI to Directive 67/548/EEC save where contrary requirements for dangerous preparations are specified in separate Directives.

92. One or both of the following procedures cause classification of preparations

- Evaluation of test results and application of criteria of Annex VI to Directive 67/548/EEC. Testing is not allowed for preparations containing carcinogenic, mutagenic or toxic to reproduction substances.

- application of the conventional method based on classification of component substances and their concentrations in a preparation.

- if it can be demonstrated that toxicological effects on man based on epidemiological findings, by scientifically valid case studies or by statistically backed experience such as the assessment of data from poison information units or occupational diseases would differ from those deriving from the procedures of classification than the preparation must be classified according to the effects on humans.

Classification of mixtures [seen in humans] according to Directive on Dangerous Preparations/EU

93. Health hazards: The classification of mixtures can be carried out on the basis of the results of appropriate animal tests, or by applying the conventional method. Where it can be demonstrated that effects differ from those determined by either one or both methods, the classification must be based on the effects on humans.

94. The appropriate test methods are described in the Annex V to Directive 67/548/EEC.

95. The application of the conventional method according to Directive 88/379/EEC is based on a principle that the conventional method should provide a similar result of hazard assessment as testing of a preparation ensuring a high level of protection envisaged by this regulation. The method avoids using test animals and provides an inexpensive way of assessment in particular for the use by small and medium size enterprises.

96. All toxicological end points for preparations shall be assessed either on the basis of test results or by the conventional method. If the preparation has been tested for some endpoints, the test results are used for classification for those end points. All other end points have to be assessed by applying the conventional method. However, carcinogenic, mutagenic or toxic to reproduction properties should always

be determined by the conventional method rather than animal testing, because the results of such tests are not considered to be sufficiently reliable.

97. The conventional method is based on following fundamentals:

- classification of the substance
- concentration of the substance in the mixture
- concentration limit for the classification

98. The application of the conventional method requires first classification of substances present in the preparation. The substances are classified either in Annex I to Directive 67/548/EEC (harmonised classification) or provisionally by the person responsible for placing on the market of the substance or preparation on the basis of available data and application of classification criteria of Annex VI to Directive 67/548/EEC.

99. The data that are available for different end points shall be used. If the data for substances are based on tests, which have been carried out according to test guidelines the data are directly applicable for classification. If the data are not according to test guidelines the value of the data have to be assessed for the classification purposes (expert judgement).

100. By the evaluation of the dangerous properties of a preparation by the conventional method the calculation should be done by using the real concentration of the substance in the preparation. The substances are taken into account if the cut-off limits for classification are exceeded. When the additivity calculation for classification is applicable the concentrations of substances to be taken into consideration are 0.1% for very toxic and toxic substances and 1% for corrosive, irritant and harmful substances.

101. The concentration limits for classification are applied when the component substances are first classified. General concentration limits for classification of preparations are specified for all toxicological end points by Directive 88/379/EEC. In the case of substances for which individual concentrations limits are specified in Annex I of Directive 67/548/EEC, mixtures containing these substances should be classified by reference to those substance-specific limits. In these cases the substance-specific limits should be used. In any other cases the general limits laid down in the Directive 88/379 are applicable.

102. If no data are available for certain end points the preparation is not classified for those end points.

103. For some of the end points e.g. for acute toxicity decreasing ranges of concentration limits are used. The rationale behind this is that below the general concentration limit for an acute lethal effect like very toxic, the preparation can still be toxic or harmful at an even lower concentration.

104. The same principle applies to a property like corrosivity, where lower concentrations limits are also applied to take into account irritation effects.

105. A similar conventional method is proposed for the assessment of environmental hazards in the proposal for the new Directive on dangerous preparations. The applicability of test results for properties dangerous for the environment is restricted for the reason that certain tests are not suitable for mixtures.

106. Physico-chemical hazards are assessed by tests.

107. The result of the classification is the identification of the category of hazards to which the preparation is attached and which indications of special risks are associated with the preparation, for

example, C, R34: Corrosive, causes burns, N, R50: dangerous to the environment, very toxic to aquatic organisms. The information on the label of a dangerous preparation is directly derived from classification

Concentration limits for classification

108. The concentration limits for the classification of a preparation for different endpoints of health effects are described in tables 1 and 2 for liquids and solids and tables 1a and 2a for gases. A similar conventional method to that described for health effects is proposed for the assessment of environmental hazards in the proposal for the new Directive on dangerous preparations. The concentration limits for the classification of preparations for the environmental effects are described in table 3 according to the new proposal for the Directive of dangerous preparations.

Table 1 Concentration limits for classification of preparations (solids and liquids) for their acute lethal effects and corrosive or irritant effects, properties for which additivity may apply

Classification of the substance	Classification of the preparation			Classification of the preparation			
	T+, R26, R27, R28 Acute lethal effects	T, R23, R24, R25 Acute lethal effects	Xn, R20, R21, R22 Acute lethal effects	C, R35 Severe burns	C, R34 Burns	Xi, R41 Serious damage to eyes	Xi, R36, R37, R38 Irritates eyes, respiratory system or skin
T+, R26, R, 27, R28 Acute lethal effects	conc. ≥ 7%	1% ≤ conc. < 7%	0.1% ≤ conc. < 1%	-	-	-	-
T, R23, R24, R25 Acute lethal effects	-	conc. ≥ 25%	3% ≤ conc. < 25%	-	-	-	-
Xn, R20, R21, R22 Acute lethal effects	-	-	conc. ≥ 25%	-	-	-	-
C, R35 Severe burns	-	-	-	conc. ≥ 10 %	5 % ≤ conc. < 10 %	conc. = 10%	1% ≤ conc.< 5% R36/38
Xi, R41 Serious damage to eyes	-	-	-	-	-	conc. ≥ 10%	5% ≤ conc. < 10% R36
Xi, R36, R37, R38 Irritates eyes, respiratory system or skin	-	-	-	-	-	-	conc. ≥ 20% R36, R37, R38
C, R34 Burns	-	-	-	-	conc. ≥ 10%	conc. = 10%	5% ≤ conc. < 10% R36/38

Notes to Table 1: Concentration limits for classification of preparations (solids and liquids) for their acute lethal effects and corrosive or irritant effects, properties for which additivity may apply

- The table shows that an acute lethal effect or a local effect (corrosive/irritant) is considered to be diluted with a diluted concentration.

- The properties of acute lethal toxicity expressed by classification of component substances as T+, T and Xn with appropriate R-phrases are considered to be additive. The same applies to corrosive and irritant properties expressed by C or Xi with appropriate phrases. This is justified by the assumption that the mechanisms causing these effects are similar.

- If the concentration of a component substance does not exceed the limits for classification given in the table the concentrations of similar substances are summarised and the sum of concentrations is compared with the classification limit. This principle can be expressed by a formula in a general form:

$$\sum \frac{p_i}{L_i} \geq 1$$

where p_i = the concentration of a dangerous substance in a preparation, L_i = the concentration limit for classification.

- The lowest concentrations to be taken into consideration are for very toxic and toxic substances 0.1 % and for harmful, corrosive and irritant substances 1 % unless lower values are given in Annex I to Directive 67/548/EEC.

- An application of the formula can be illustrated by an example:

  a preparation contains:

  - 0.5 % of a toxic substance A with T R25,
  - 1 % of a toxic substance B with T R25 and
  - 20 % of a harmful substance C with Xn R22.

- Any concentration of the components does not exceed the classification limit as toxic or harmful. The formula is then applied:

$$\frac{P_A}{L_{Xn}} + \frac{P_B}{L_{Xn}} + \frac{P_C}{L_{Xn}} =$$

$$\frac{0.5}{3} + \frac{1}{3} + \frac{20}{25} = 1.3 \geq 1$$

The sum is $\geq$ 1 which means that the preparation is classified as harmful Xn with R22.

Table 2 Concentration limits for classification of preparations (solids and liquids) for other than acute lethal effects and corrosive or irritant effects, properties for which additivity does not apply

Classification of the substance	Classification of the preparation												
	T+, R39 Non- lethal irreversible effects	T, R39 Non- lethal irreversible effects	Xn, R40 Non- lethal irreversible effects	T, R48 Severe effects after repeated or prolonged exposure	Xn, R48 Severe effects after repeated or prolonged exposure	Xn, R42 Sensitising effects, inhalation	Xi, R43 Sensitising effects, skin	Carc. Cat. 1 or 2	Carc. Cat. 3	Muta. Cat. 1 or 2	Muta. Cat. 3	Repro tox Cat. 1 or 2	Repro tox. Cat. 3
T+, R39, Non-lethal irreversible effects	conc. ≥ 10%	1% ≤ conc. < 10%	0.1% ≤ conc. < 1%	-	-	-	-	-	-	-	-	-	-
T, R39 Non-lethal irreversible effects	-	conc. ≥ 10%	1 % ≤ conc. < 10%	-	-		-	-	-	-	-	-	-
Xn, R40 Non-lethal irreversible effects	-	-	Conc. ≥ 10%	-	-	-	-	-	-	-	-	-	-
T, R48 Severe effects after repeated or prolonged exposure	-	-	-	conc. ≥ 10%	1% ≤ conc. < 10%	-	-	-	-	-	-	-	-

Table 2 Concentration limits for classification of preparations (solids and liquids) for other than acute lethal effects and corrosive or irritant effects, properties for which additivity does not apply (cont.)

Classification of the substance	Classification of the preparation												
	T+, R39 Non- lethal irreversible effects	T, R39 Non- lethal irreversible effects	Xn, R40 Non- lethal irreversible effects	T, R48 Severe effects after repeated or prolonged exposure	Xn, R48 Severe effects after repeated or prolonged exposure	Xn, R42 Sensitising effects, inhalation	Xi, R43 Sensitising effects, skin	Carc. Cat. 1 or 2	Carc. Cat. 3	Muta Cat. 1 or 2	Muta Cat. 3	Repro tox Cat. 1 or 2	Repro tox cat. 3
Xn, R48 Severe effects after repeated or prolonged exposure	-	-	-	-	conc. ≥ 10%	-	-	-	-	-	-	-	-
Xn, R42 Sensitizing effects, inhalation	-	-	-	-	-	conc. ≥ 1%	-	-	-	-	-	-	-
Xi, R43 Sensitizing effects, skin	-	-	-	-	-	-	Conc. ≥ 1%	-	-	-	-	-	-
Carc., cat. 1 or 2	-	-	-	-	-	-	-	conc. ≥ 0.1%	-	-	-	-	-
Carc., cat. 3	-	-	-	-	-	-	-	-	Conc. ≥ 1%	-	-	-	-

Table 2 Concentration limits for classification of preparations (solids and liquids) for other than acute lethal effects and corrosive or irritant effects, properties for which additivity does not apply (cont.)

Classification of the substance	Classification of the preparation												
	T+, R39 Non- lethal irreversible effects	T, R39 Non- lethal irreversible effects	Xn, R40 Non- lethal irreversi ble effects	T, R48 Severe effects after repeated or prolonged exposure	Xn, R48 Severe effects after repeated or prolonged exposure	Xn, R42 Sensitizing effects, inhalation	Xi, R43 Sensitizing effects, skin	Carc. Cat. 1 or 2	Carc. Cat. 3	Muta. Cat. 1 or 2	Muta. Cat. 3	Repro tox Cat. 1 or 2	Repro tox cat. 3
Muta. cat. 1 or 2	-	-	-	-	-	-	-	-	-	conc. ≥ 0.1%	-	-	-
Muta. cat. 3	-	-	-	-	-	-	-	-	-	-	conc. ≥ 1%	-	-
Reprotox. cat. 1 or 2	-	-	-	-	-	-	-	-	-	-	-	conc. ≥0.5%	-
Reprotox. cat. 3	-	-	-	-	-	-	-	-	-	-	-	-	conc. ≥ 5%

Notes to Table 2 Concentration limits for classification of preparations (solids and liquids) for other than acute lethal effects and corrosive or irritant effects, properties for which additivity does not apply

- The additivity does not apply to those health effects which are listed in table 2. Concentration of a component substance is compared directly with the classification limit of table 2. If the limit is exceeded the preparation is classified, if it is not exceeded that preparation is not classified.

- The irreversible effects after single exposure and effects of long-term or repeated exposure are categorised according to the dose causing the effect. Again with diluted concentration the effects are also linearly diluted which results in milder classification in diluted concentrations.

- Both skin and respiratory sensitisers are recognised in the EU system to belong to the same category of danger and as a consequence, only one limit is applied for classification.

- The categorisation of carcinogens, mutagens and toxic to reproduction substances is based on evidence, not on severity of effects. Only one limit is applied for classification in each category of c/m/r.

Table 3 Concentration limits for classification of preparations (solids and liquids) for environmental effects
Acute aquatic toxicity and long-term adverse effects, dangerous for the ozone layer

Classification of the substance	Classification of the preparation								
	N, R50-53 Very toxic to aquatic organisms and may cause long-term adverse effects	N, R51-53 Toxic to aquatic organisms and may cause long-term adverse effects	R52-53 Harmful to aquatic organisms and may cause long-term adverse effects	N, R50 Very toxic to aquatic organisms	R52 Harmful to aquatic organisms	R53 Long term adverse effects	N, R59 Dangerous for the ozone layer	R59 Dangerous for the ozone layer	Note
1. N, R50-53 Very toxic to aquatic organisms and may cause long-term adverse effects	Conc. $\geq$ 25 %	2.5 $\leq$ conc. < 25 %	0.25 $\leq$ conc. < 2.5 %						Additivity applies
2. N, R51-53 Toxic to aquatic organisms and may cause long-term adverse effects		Conc. $\geq$ 25 %	2.5 $\leq$ conc. < 25 %						Additivity applies
3. R52-53 Harmful to aquatic organisms and may cause long term adverse effects			conc. $\geq$ 25 %						Additivity applies
4. N, R50 Very toxic to aquatic organisms				conc. $\geq$ 25%					Additivity applies

Table 3 Concentration limits for classification of preparations (solids and liquids) for environmental effects Acute aquatic toxicity and long-term adverse effects, dangerous for the ozone layer (cont.)

Classification of the substance	Classification of the preparation								
5. R52 Harmful to aquatic organisms					**Conc. ≥25 %**				**Additivity applies**
6. R53 Long term adverse effects						**Conc. ≥ 25 %**			**Additivity applies**
7. N, R59 Dangerous for the ozone layer							**Conc. ≥ 0.1 %**		**-**
8. R59 Dangerous for the ozone layer								**Conc. ≥ 0.1 %**	**-**

If the concentration of a component substance does not exceed the limits for classification given in the table the concentrations of similar substances are summarised and the sum of concentrations is compared with the classification limit.

Notes to Table 3 Concentration limits for classification of preparations (solids and liquids) for environmental effects, Acute aquatic toxicity and long-term adverse effects, dangerous for the ozone layer

- This principle can be expressed by a formula in a general form:

$$\sum \frac{p_i}{L_i} \geq 1$$

where:

P_i = the concentration of a substance dangerous for the environment in a preparation,
L_i = the concentration limit for classification.

- The additivity is restricted to certain cases. Concentrations of components of the following boxes of table 3 can be summarised:
  - boxes 1 to 3 to assess the acute aquatic toxicity in combination with long term adverse effects
  - boxes 1 and 4 to assess very toxic acute effects to the aquatic organisms
  - box 5 to assess harmful acute effects to the aquatic organisms
  - boxes 1, 2, 3 and 6 to assess adverse long term effects to the aquatic environment

  Additivy is not applied to substances which may cause dangers for the ozone layer.

- The lowest concentrations to be taken into consideration are 0.1 % for substances which are very toxic or toxic to aquatic organisms, whether or not in combination with long term adverse effects in aquatic environment. The lowest concentrations to be taken into consideration are 1 % for substances which are harmful to aquatic organisms, and/or which pose long-term adverse effects in aquatic environment, unless lower values are given in Annex 1 to Directive 67/548/EEC.

- An application of the formula can be illustrated by an example: A preparation contains:

  a substance A which is very toxic to aquatic organisms and may cause long-term adverse effects in the aquatic environment. The classification is N, R50-53 and concentration 0.1%

  a substance B which is toxic to aquatic organisms and may cause long-term adverse effects in the aquatic environment. The classification is N, R51-53 and the concentration 2%

  a substance C which is harmful to aquatic organisms and may cause long term adverse effects in the aquatic environment. The classification is R52-53 and the concentration 20%

Any concentration of the individual components does not exceed the classification limit as dangerous for the environment. The formula is then applied:

$$\frac{P_A}{L_{R52-53}} + \frac{P_B}{L_{R52-53}} + \frac{P_C}{L_{R52-53}} > 1$$

The sum is >1 which means that the preparation is classified as harmful to aquatic organisms and may cause long-term adverse effects in the aquatic environment, R52-53.

Table 4 Concentration limits for classification of preparations (gases) for their acute lethal effects and corrosive or irritant effects, properties for which additivity may apply

Classification of the substance	Classification of the preparation			Classification of the preparation			
	T+, R26, R27, R28 Acute lethal effects	T, R23, R24, R25 Acute lethal effects	Xn, R20, R21, R22 Acute lethal effects	C, R35 Severe burns	C, R34 Burns	Xi, R41 Serious damage to eyes	Xi, R36, R37, R38 Irritates eyes, respiratory system or skin
T+, R26, R, 27, R28 Acute lethal effects	conc. ≥ 1 %	0.2 % ≤ conc. < 1 %	0.02 % ≤ conc. < 0.2%	-	-	-	-
T, R23, R24, R25 Acute lethal effects	-	conc. ≥ 5 %	0.5 % ≤ conc. < 5 %	-	-	-	-
Xn, R20, R21, R22 Acute lethal effects	-	-	conc. ≥ 5 %	-	-	-	-
C, R35 Severe burns	-	-	-	conc. ≥ 1 %	0.2 % ≤ conc. < 1 %	conc. 0.2 %	0.02 % ≤ conc.< 0.2 %
C, R34 Burns	-	-	-	-	conc. ≥ 5 %	conc. 5 %	0.5 % ≤ conc. < 5 %
Xi, R41 Serious damage to eyes	-	-	-	-	-	conc. ≥ 5 %	0.5 % ≤ conc. < 5 %
Xi, R36, R37, R38 Irritates eyes, respiratory system or skin	-	-	-	-	-	-	

Table 5 Concentration limits for classification of preparations (gases) for other than acute lethal effects and corrosive or irritant effects, properties for which additivity does not apply

Classification of the substance	Classification of the preparation												
	T+, R39 Non-lethal irreversible effects	T, R39 Non-lethal irreversible effects	Xn, R40 Non-lethal irreversible effects	T, R48 Severe effects after repeated or prolonged exposure	Xn, R48 Severe effects after repeated or prolonged exposure	Xn, R42 Sensitising effects, inhalation	Xi, R43 Sensitising effects, skin	Carc. cat. 1 or 2	Carc. cat. 3	Muta. cat 1 or 2	Muta. cat. 3	Repro tox cat. 1 or 2	Repro tox cat. 3
T+, R39, Non-lethal irreversible effects	conc. $\geq$ 1%	0.2% $\leq$ conc. < 1%	0.02% $\leq$ conc. < 0.2%	-	-	-	-	-	-	-	-	-	-
T, R39 Non-lethal irreversible effects	-	Conc. $\geq$ 5%	0.5% $\leq$ conc. < 5%	-	-	-	-	-	-	-	-	-	-
Xn, R40 Non-lethal irreversible effects	-	-	conc. $\geq$ 5%	-	-	-	-	-	-	-	-	-	-
T, R48 Severe effects after repeated or prolonged exposure	-	-	-	conc. $\geq$ 5%	0.5 % $\leq$ conc. < 5%	-	-	-	-	-	-	-	-

Cont. Table 5 Concentration limits for classification of preparations (gases) for other than acute lethal effects and corrosive or irritant effects, properties for which additivity does not apply (cont.)

Classification of the substance	Classification of the preparation												
	T+, R39 Non-lethal irreversible effects	T, R39 Non- lethal irreversible effects	Xn, R40 Non- lethal irreversible effects	T, R48 Severe effects after repeated or prolonged exposure	Xn, R48 Severe effects after repeated or prolonged exposure	Xn, R42 Sensitising effects, inhalation	Xi, R42/43 Sensitising effects, skin	Carc., cat. 1 or 2	Carc., cat. 3	Muta. cat. 1 or 2	Muta. cat. 3	Repro tox cat.1 or 2	Repro tox cat. 3
Xn, R48 Severe effects after repeated or prolonged exposure	-	-	-	-	conc. $\geq$ 5%	-	-	-	-	-	-	-	-
Xn, R48 Severe effects after repeated or prolonged exposure	-	-	-	-	conc. $\geq$ 5%	-	-	-	-	-	-	-	-
Xn, R42 Sensitising effects, inhalation	-	-	-	-	-	conc. $\geq$ 0.2%	-	-	-	-	-	-	-
Xi, R43 Sensitising effects, skin	-	-	-	-	-	-	conc. $\geq$ 0.2%	-	-	-	-	-	-

Table 5 Concentration limits for classification of preparations (gases) for other than acute lethal effects and corrosive or irritant effects, properties for which additivity does not apply (cont.)

Classification of the substance	Classification of the preparation												
	T+, R39 Non-lethal irreversible effects	T, R39 Non-lethal irreversible effects	Xn, R40 Non-lethal irreversible effects	T, R48 Severe effects after repeated or prolonged exposure	Xn, R48 Severe effects after repeated or prolonged exposure	Xn, R42 Sensitising effects, inhalation	Xi, R43 Sensitising effects, skin	Carc. cat. 1 or 2	Carc. cat. 3	Muta. cat. 1 or 2	Muta. cat. 3	Repro tox cat. 1 or 2	Repr tox cat. 3
Carc., cat. 1 or 2	-	-	-	-	-	-	-	conc. ≥ 0.1%	-	-	-	-	-
Carc., cat. 3	-	-	-	-	-	-	-	-	conc. ≥ 1%	-	-	-	-
Muta. cat. 1 or 2	-	-	-	-	-	-	-	-	-	conc. ≥ 0.1%	-	-	-
Muta. cat. 3	-	-	-	-	-	-	-	-	-	-	conc. ≥ 1%	-	-
Reprotox. cat. 1 or 2	-	-	-	-	-	-	-	-	-	-	-	conc. ≥0.2 %	-
Reprotox. cat. 3	-	-	-	-	-	-	-	-	-	-	-	-	conc. ≥ 1%

Role of test data

109. Tested Mixtures: In cases where appropriate data are available hazard classification based on test data overrule those from the conventional method (standardised approach). This does not apply to cases where the preparation contains substances which are classified as carcinogenic, mutagenic or toxic to reproduction. The test results for mixtures containing substances with carcinogenic, mutagenic and toxic to reproduction properties are not accepted for hazard classification. This is due to the way tests for a substance for these endpoints are designed. In order to explore the worst case situation and to reveal the potential effects when extrapolating the results to humans, the test system for an individual substance is optimised in different ways. For example the dose is chosen so as to be the maximal tolerated dose and the number of animals in the test groups is chosen so as to give sufficient statistical power for the test to detect an effect for an individual substance.

110. If a mixture is tested the dose of a (potentially) carcinogenic, mutagenic or reproductive toxic substance can become unacceptably low. In that case the test system will not be sufficiently sensitive and these potential toxic effects will not be revealed. It is also difficult to interpret the test results when testing a mixture; for example it may not be possible to know which component has caused a certain effect. Besides these arguments the testing of mixtures for these endpoints would lead to a big increase in the use of test animals.

111. Incomplete Data Set: The classification is carried out on the basis of test data where the test data are available for the end point. All other end points are then assessed by applying the conventional method (standardised approach).

112. Bridging Data/Extrapolation: If a preparation has been tested for its health effects, the composition of the preparation may vary according to the following table without having to carry out a new assessment. If the variation of concentration of constituents is greater, the assessment shall be carried out again either by testing or by application of the conventional method (standardised approach). A new assessment (either by testing or by conventional method) shall be carried out if any of the constituents is substituted or other components are added. This will apply unless there is valid scientific justification for considering that re-evaluation of the hazard will not result in a change of classification.

Table 6 EU Permitted Concentration Variations

Initial concentration range of the constituent (w/w %)	Permitted variation in initial concentration of the constituent
Conc. < 2.5 %	± 15 % [30 %]#)
2.5 % < Conc. = 10 %	± 10 % [20 %]#)
10 % <Conc. = 25 %	± 6 % [10 %]#)
25 % < Conc. = 50 %*)	± 5 % [5 %]#)
50 % <Conc. =100 %*)	± 2.5 % [5 %]#)

#) The concentration will be changed according to the new Directive on Dangerous Preparations.

*) The range will be changed according to the new Directive on dangerous preparations to 25-100 %

113. Other Considerations: Where it can be demonstrated by epidemiological studies, by scientifically valid case studies or by statistically backed experience that toxicological effects differ from those suggested by application of the conventional method or by testing then the preparation shall be classified

according to its effects on man. Also effects such as potentiation and antagonism of the component substances shall be taken into consideration in the classification in cases, where application of the conventional method would not give a correct classification for the mixture.

114. Structure activity relationship (SAR) may be applied as supportive evidence in the assessment of mixtures only for component substances when the conventional method is applied for the classification of the mixtures as a whole. Application of SAR method to substances is rather limited. Advice for application of QSAR will be given by the revision of Annex VI to directive 67/548/EEC (25th ATP to Directive 67/548/EEC).

Role of regional legislation

115. The Treaties establishing the European Communities provide the overarching legislative framework for introducing more specific measures into Member State's territories in those area where the Community has competence. These measures can be introduced by various routes notably through Regulations (which are directly applicable in Member States); through Council Directives (where Member States are required to transpose the directive into national legislation): or through Commission Directives. Commission Directives provide a simpler means for addressing issues of scientific detail and adaptation to technical progress. Authority to agree Commission Directives is delegated to official level and they are not subject to political agreement through the full European Parliamentary process.

116. There are a number of Treaty base options (e.g. Article 118a worker protection, Article 100a harmonisation, Article 130 r, s and t environmental protection) for introducing regulations or directives selected on the basis of the subject matter and whether it is feasible to set minimum or harmonised standards in a particular area. Treaty articles are not mutually exclusive so for example worker protection or public health issues may be a primary consideration under a harmonisation directive. Additionally as the treaty bases are closely inter-linked legislative proposals in similar subject areas need to be consistent and compatible to support the broader Community objectives.

117. European Community legislation places obligations on Member States regulatory authorities, employers, employees and economic operators.

Information on countries or regions outside EU applying the EU system

118. Non EU blocs operating/applying the EU system for the classification, packaging and labelling of dangerous preparations include the major Eastern European states who have begun to implement the EU system in readiness for possible entry to the Union. Viz Estonia, Latvia, Lithuania, Poland, Czech Republic, Slovakia, Hungary, Slovenia, Romania, Bulgaria. Similarly Cyprus have also applied for membership of the EU.

119. Australia has adopted chemicals legislation which follows the EU system, but there is provision for testing all endpoints.

120. Norway and Iceland comply with the EU system according to the agreement on the European Economic Area with minor exemptions. Switzerland is in the process of transforming the national legislation on the basis of the EU model.

TRANSPORT: UNCETDG

121. Substances (including mixtures and solutions) and articles are assigned to one of nine classes according to the hazard or the most predominant of the hazards they present. Some of these classes are subdivided into divisions. With regard to health and environmental hazards the following classes and divisions are relevant : Division 2.3: Toxic gases Division 6.1: Toxic substances Division 6.2: Infectious substances Class 8 : Corrosive substances Class 9 : Miscellaneous dangerous substances and articles.

General

122. A mixture (or solution) containing a single dangerous substance listed in the Dangerous Goods List is classified as the dangerous substance unless: a) the mixture is specifically identified in the Dangerous Goods List b) the entry for the dangerous substance in the Dangerous Goods List specifically indicates that it applies only to the pure substance c) the hazard characteristics of the mixture are different from that of the pure substance d) the measures to be taken in emergencies are different.

123. In those other cases, except the one described in a), the mixture shall be classified under the appropriate "generic" or "not otherwise specified" (n.o.s.) entry. Generic entries cover well defined group of substances (e.g. "perfumery product") ; specific n.o.s. entries cover groups of substances of a particular chemical or technical nature (e.g. "barium compounds n.o.s.") ; general n.o.s. entries cover group of substances meeting the criteria of one or more classes or divisions (e.g. "toxic liquid, organic, n.o.s.").

124. A mixture containing one or more dangerous substances is not classified as dangerous if the characteristics of the mixture are such that they do not meet the classification criteria (including human experience criteria) for any class.

Gas mixtures

125. A gas mixture is classified as toxic (or corrosive) if the LC_{50} of the mixture is equal or lower of the level established for the classification of toxic gases, the LC_{50} being determined : -by tests, or -by calculation method (on the basis of the LC_{50} of the components and of their molar fraction) : when the LC_{50} values are unknown the lowest LC_{50} value of substances of similar physiological and chemical effects can be used .

Mixtures of liquids toxic by inhalation

126. If the LC_{50} data are available for each of the toxic substances, the LC_{50} of the mixture is evaluated on the basis of the LC_{50} for each substance and of its molar fraction. Otherwise a simplified threshold toxicity test (on albino rats) is allowed.

Mixtures of toxic (oral and dermal toxicity) substances

127. If a mixture contain only one toxic substance, whose LD_{50} is known, the mixture is classified on the basis of the LD_{50} evaluated as: (LD_{50} of the substance) x 100/ % in mass. If a mixture contain more

than one toxic substance, the preferred method is to obtain toxicity data on the mixture. If reliable, accurate data are not available, the mixture is classified assuming that the more toxic substance is present in the same concentration as the total concentration of all toxic constituents, or on the basis of a formula taking care of the LD_{50} of the components and of their molar fraction.

Environmental hazards

128. In the UNRTDG classification for environmental effects is not directly addressed. In the IMDG Code (maritime transport) mixtures are classified as "marine pollutants" if they contain more than 10% of a marine pollutant or more than 1% of a severe marine pollutant.

129. In RID/ADR (land transport in Europe) if a mixture contain only one environmental hazardous substance, whose LC_{50} is known, the mixture is classified as environmentally hazardous on the basis of the LC_{50} (for fishes, daphnia or algae) evaluated as: (LC_{50} of the substance) x 100/% in mass.

Wastes

130. Wastes are classified according to the same rules for classification as other substances or mixtures.

Special cases

131. For some entries in the Dangerous Goods List there is a Special Provision where limits of concentration are specified for the dangerous component, so that under that limit the mixture is no more classified as dangerous (e.g. "An aqueous solution containing not more than 24 % alcohol by volume is not subject to these regulations").

US: OSHA HCS

Standardised approach

132. US OSHA Hazard Communication Standard (HCS): Where test data are not available, mixtures are assumed to have the same health hazards as do the components which comprise one percent (by weight or volume) or greater of the mixture as a whole.

133. Exceptions: Mixtures are considered carcinogenic for purposes of hazard communication when they comprise 0.1% (by weight or volume) or greater of the mixture as a whole.

134. If there is evidence that a component present in concentrations less than one percent (0.1% for carcinogens) can be released in concentrations that would exceed OSHA’s established permissible exposure limits or ACGIH’s recommended exposure limits, or presents a health hazard to employees in those lower concentrations, the mixture is assumed to be hazardous for purposes of hazard communication.

Role of test data

135. Tested Mixtures: If test data are available on the mixture as a whole, the classification is to be based on the data. Chemicals may have test data for some endpoints and not others. If there are no data for a particular end point, the classification for that health effect would be based on the standardised approach.

136. Incomplete Data Set: Classification is based on test data where available, and the end points where no data are available are classified based on the standardised approach. If the toxicity of components is unknown, there is no requirement to cover them. The HCS does not require testing, and structure-activity relationships are also not a required part of the evaluation process.

137. Bridging Data/Extrapolation: No. The classification is to either be based on actual test data or on the standardised approach.

138. Similar Mixtures: There is a limited exception under the HCS which does not fit neatly into the 3 categories of mixtures outlined. Where there are complex mixtures with similar contents and hazards, a single data sheet may be used to convey the hazards of more than one mixture. For example, petroleum streams may vary slightly in composition in terms of the percentage of a certain ingredient, but the hazard of the mixture would not be different because of that variation. In that situation, OSHA would allow the manufacturer to use the same data sheet even though the composition may vary. This is expected to be applied only in very narrow circumstances. Under the HCS, negative data may never negate the finding of hazard. Chemical manufacturers and importers may report such data on the MSDS, as well as indicate their interpretations of its relevance, but the MSDS must be provided and the positive data must be reported.

Role of federal legislation

139. Under the OSH Act there is intent to pre-empt state laws in areas where federal OSHA has promulgated occupational safety and health laws. Presently, there are several states (CA, NJ, PA) which have laws promulgated for related purposes (environmental protection, drinking water safety, etc.) that have hazard communication requirements in addition to the federal requirements. The HCS applies in the workplace when employees are exposed to a chemical under normal conditions of use or in a foreseeable emergency. There are no special considerations for susceptible populations. Generally speaking, OSHA's policy has always been to protect all types of workers under its standards rather than trying to separate out certain parts of the worker population. In addition, children and the elderly are not usually part of the worker population.

140. Impurities and contaminants are treated as are any other component. There are no special considerations for synergistic and antagonistic effects of ingredients in a mixture, but it would be expected that these would be taken into account when known. As already noted, where mixtures are similar in concentration, hazard, and content, the HCS allows a single MSDS to suffice to meet the requirements. Thus slight reformulations that don't change the overall hazard should not result in new MSDSs. Exposure, potency, and seriousness of effect are not taken into consideration under the HCS. The scheme is used for hazard communication purposes only, that is, labels, MSDSs and training. There is a link to community right-to-know provisions implemented under EPA requirements. Other risk management approaches in OSHA's standards include a full range of protective measures, from engineering controls to personal protective equipment. The chemical manufacturer or importer conducting the hazard determination is responsible for interpreting and using the data available. The hazard determination is to be based on all available evidence, both animal and human data. The chemical manufacturer or importer is held responsible for identifying the required data, and for ensuring that the data meets the standard's requirements to be conducted according to scientific principles and having statistically significant results. If there is one such study that indicates an adverse health effect, the substance or mixture or component of a mixture is considered to be hazardous. Professional judgement is applied to determining the quality of the data and whether it meets the specified criteria. Otherwise, there is little professional judgement applied to untested mixtures since the percentage cut-off rule is applicable. OSHA may conduct its own hazard determination in order to ascertain whether the one performed by a chemical manufacturer or importer is appropriately done. If we find that it is not, they may be cited for non-compliance.

141. Information provided by companies may relate to the mixture as a whole or to individual components, based upon the availability of test data. OSHA does not require testing - all determinations are based on available data. MSDSs provide key information to downstream employers in designing and implementing effective employee protection programs. Before the HCS was adopted, such employers frequently had no information about the components of a mixture, or the potential hazards of products they are using. While the manufacturer or importer can provide such information about the products, it is the employer who knows how the product is used in the workplace, what other exposures there may be, and what protective measures are available. Thus the concept of risk is best introduced by the using employer with access to all of this information. That risk concept translates to selection and implementation of the protective measures best suited to the particular combination of hazards and exposure levels in the workplace.

Table 7 Workplace
Untested Mixture Classification Concentration cut-off Values (%) By Toxicity End Point

END POINT	***WHMIS***	***EU***		***OSHA HCS***	***UNCETDG***	
		solid/liquid	gas		solid/liquid	gas
Acute Toxicity (LD_{50} & LC_{50})	1	0.1, 3, 7, 25	0.02,0.2, 0.5, 5	1	no %	no %
Carcinogenicity	0.1	0.1, 1	0.02, 0.2	0.1	NA	NA
Reproductive Toxicity	0.1	0.5, 5	0.2, 1	1	NA	NA
Skin Sensitisation	1	1	0.2	1	NA	NA
Respiratory Sensitisation	0.1	1	0.2	1	NA	NA
Eye Irritation	1	5, 20	0.5, 5,	1	NA	NA
Skin Irritation	1	5, 10, 20	0.5, 5	1	NA	NA
Corrosion to Skin	1	1, 5, 10	0.2, 1, 5	1	NA	no %
Corrosion to Eyes	1	5, 10	0.5, 5	1	NA	NA
Germ Cell Mutagenicity	0.1	0.1	0.1	1	NA	NA
Somatic Cell Mutagenicity	1	1	1	1	NA	NA
Target Organ -Chronic Toxicity	1	1, 10	0.5, 5	1	NA	NA

142. In the European system for classification of mixtures cut-off concentration limits for component substances are set for classification. When a preparation is classified on the basis of acute toxicity, corrosive/irritant effects or effects dangerous for the aquatic environment the concentrations of components not exceeding alone the limits for classification are summed-up and the sum is compared with the classification limit. (additivity principle). For the other end points each component substance is compared individually with respect to its end point limit to classify the mixture accordingly. However, when substance specific concentration limits exist for individual components of the mixture in Annex I to Directive 67/548/EE, these limits must be used when applying the standardised method.

143. Further more, the agreed classification criteria recognise the dilution of effects by specifying different cut-off limits for acute toxicity and for effects dangerous for the aquatic environment as well as for scores (or time dependent effects) for corrosive/irritant effects. These criteria would be followed if mixtures were tested in different concentrations of same compounds. (dilution principle)

144. The lowest concentrations of component substances that are taken into consideration are specified for application of the classification system for mixtures and in particular for the application of additivity principle.

145. In the case of acute toxic substances for instance, the value to take this end point into consideration is 0.1% whereas the cut-off limits for classification of the mixture for its acute toxicity is 3%.

146. The limits are specified for end points in the new Directive on dangerous preparations, but are included also in the present Directive. The lowest concentrations that are taken into consideration (unless lower concentration limits are specified in Annex I to Directive 67/548/EEC or in the Annexes of preparations Directive) are presented in the following table:

Table 8

Category of danger of the substance	Concentrations to take into consideration	
	Gaseous preparations %vol/vol	Other preparations % w/w
Very toxic	0.02	0.1
Toxic	0.02	0.1
Carcinogenic Category 1 and 2	0.02	0.1
Mutagenic Catgerory 1 and 2	0.02	0.1
Toxic for reproduction Category 1 and 2	0.02	0.1
Harmful	0.2	1
Corrosive	0.02	1
Irritant	0.2	1
Sensitising	0.2	1
Carcinogenic Category 3	0.2	1
Mutagenic Category 3	0.2	1
Toxic for reproduction Category 3	0.2	1
Dangerous for the environment, N		0.1
Dangerous for the environment	0.1	0.1
Ozone Dangerous for the environment		1

PESTICIDES

147. A comparison of the major classification systems for pesticides is given in Appendix II Table IV-4. In all systems, available test data on active ingredient, pesticide mixtures, formulations or marketable preparations are used to classify pesticide mixtures. Acute toxicity (oral, dermal, inhalation) end points are used for classification of mixtures in all systems. The requirement for testing skin irritation, eye irritation, sensitisation, neurotoxicity, carcinogenicity, reproductive effects and ecotoxicity vary among the systems and, in some cases, within systems depending upon the intended use of the pesticide. In the EU, if the correctness of the classification on the basis of calculation method is open to doubt, the competent authorities may require that the calculation be replaced by toxicological tests. The EU specifies the classification rules that are used by the Member State Competent Authorities for the purposes of classification. There is no standardised approach in the US or Canada for determining the hazards of an untested mixture. In Table IV-4, for example, reference is made to expert judgement, on a case-by-case basis, similarity of products and waiving of test data requirements.

Canada

148. In Canada, the *Pest Control Products Act* (PCPA) governs the registration of pesticides. Studies to identify acute hazards are performed on the active ingredient and end-use product. The active ingredient is also subjected to subchronic, chronic, reproductive and genotoxicity testing. The potential risk for the proposed use, considering risk mitigation measures such as user restrictions, education programs, protective equipment or other means determines the acceptability of the product for registration. Conditions under which the product is used are considered in the determination of risk, but foreseeable misuse is not a factor in assessing the hazard component of the risk equation.

149. In Canada, the petitioner for registration is responsible for hazard determination and proposed classification (market class designation, hazard symbols, and signal words). The regulatory authority, the Pest Management Regulatory Agency, verifies the appropriateness of the classification.

Definitions

150.

- *Substance/chemical*: chemical elements/entities and their constituents, as they occur in the natural state or produced by industry, e.g. technical grade active ingredients including impurities/contaminants resulting from the manufacturing process which can be further utilized in preparations and "chemical soups" such as creosote which may also be used in preparations. (Adapted from the EC)

- *Preparations*: a mixture or solution composed of two or more substances at least one of which is a pesticidal active ingredient; the mixture is not known to, or is not expected to chemically react (irreversibly) to form other chemical entities. (Adapted from the EC)

NB: The terms "substance" and "preparation" are not utilised in the Canadian pesticides scheme. The above two definitions represent PMRA adaptations of the EC terms. The corresponding terms used within PMRA would be "active ingredient" and "end-use product (also referred to as a formulated product), respectively.

- *Active ingredient*: that ingredient of a control product to which the effects of the control product are attributed, including a synergist, but does not include a solvent, diluent, emulsifier or component that by itself is not primarily responsible for the control effect of the control product. (Source: Regulations of the Pest Control Products Act)

- *Non-active ingredient or formulant*: a material intentionally added to a technical active ingredient during formulation of an end-use product to improve its physical characteristics, e.g., sprayability, solubility, spreadability, and stability. (Source: Registration Handbook, a PMRA document designed to provide updated information on the registration process as well as general guidance for petitioners of pesticide registration submissions.)

- *End-use product*: a product containing active ingredients(s) and usually non-active ingredients(s) that is labelled with instructions for pest control use. (Source: Registration Handbook)

Classification of pesticide mixtures

151. PMRA does not define toxicity categories/classes for classification purposes as does the United States with its four toxicity categories. But based on criteria and cut-off values (e.g. LD_{50}) a determination is made for appropriate market classification (domestic, commercial, restricted market classification). Information regarding classification of end-use products or mixtures is provided in what is known as the Registration Handbook. It contains information on market classes (for all intents and purposes representative of the Canadian classification scheme) and the associated safety criteria, cut point values for the classification of acute hazard as well as glyph or symbol usage.

Labelling

152. Regulations stipulate that pesticide labelling must contain information reflecting the nature and degree of hazard. Specific requirements for categorisation (i.e., cut-off values for toxicity classes) for acute toxicity (i.e. oral, inhalation and dermal), skin and eye irritation and sensitisation are not stated in the regulations. Identification of hazard is accomplished through the use of appropriate precautionary symbols and signal words on the label. These symbols and signal words pertain to acute toxicity and physical hazards. Consideration of factors such as the physical form of a pesticide product or the use of tamper-proof packaging can impact on the need for acute hazard labelling. It is appropriate to say, therefore, that labelling is based on a regulatory requirement to identify acute hazards, although risk considerations also play a part in some cases.

153. Products are not labelled for non-acute toxicity endpoints (carcinogenicity, reproductive toxicity, etc).

Toxicity testing

154. Acute toxicology testing is required to support registration and to provide the basis for labelling of active ingredients and mixtures. Acute oral, dermal, inhalation toxicity, skin and eye irritations, as well as skin sensitisation studies form the core battery of required tests. Acute neurotoxicity studies are required for products for which effects on the nervous system are anticipated due to chemical class (organophosphates, carbamates,) or other information. Waivers for testing are considered on a case-by-case basis taking into consideration known characteristics of the components (e.g. irritative properties), physical form (e.g. waxy or gummy resins not representing an inhalation hazard), or other scientifically sound information.

Data waivers / bridging data

155. While Canadian pesticide regulatory authorities may accept bridging data to characterise acute hazards for a mixture (formulation), the onus is on the petitioner to develop this rationale and make the necessary arrangements to use another data source (i.e., another company) for bridging purposes. PMRA must respect confidential business information when using data from one registrant's product to support a second registrant's product. It is up to the petitioner to demonstrate safety of their particular submission, thus Canadian pesticide regulatory authorities would look to the petitioner to demonstrate that the new formulant would not alter the toxicological profile of the formulation. PMRA would consider the use of existing acute toxicology data if a less toxic formulant has replaced a more toxic one or request new acute studies only for those of the studies whose results are expected to alter (e.g. irritation studies) with the new non-active ingredient. The request for the study waivers considers the fact that the properties of the new formulant may affect the overall toxicology profile, even though a comparison of the formulants may reveal that the toxicity of each is similar. Replacing a formulant to reduce eye irritation, for example, may lead to another hazard or a change in degree of an existing hazard.

156. If sufficient acute toxicity data is available for a range of concentrations of all of the ingredients in an end-use product, PMRA may be able to interpolate for toxicities of products falling within this range, providing the range of concentration falls within the same cut-off values for market classification and precautionary labelling.

157. If a petitioned product is an aqueous dilution of a product with supporting acute data, PMRA may use this data to support the petitioned product. The data would not be used as a quantitative determination of toxicity and only used in cases where there is no ambiguity with regards to the appropriate precautionary labelling. The new product would be placed in the same toxicity level as the supporting data. This approach has most merit when the well-characterised product is of low toxicity/hazard potential.

158. Where a product represents the highest hazard/toxicity level and ingredients are changed which would maintain or increase the toxicity, PMRA could use the toxicity data on the existing product keeping the new product in the highest level.

159. If a pesticide product is characterised as a dermal sensitiser, this designation will not be changed if the product is reformulated with a different concentration of the sensitising ingredient.

160. A product or active ingredient with a pH of less than 2 or greater than 11.5 should not be tested for skin or eye irritation, but will be assigned to the highest level for irritation. A product or active ingredient, which is corrosive to the skin, should not be tested for eye irritation, but will be assigned to the highest level for eye irritation.

Formulants

161. The identity and quantity of the pesticide active ingredient(s) must be disclosed on the product label according to legislation. Disclosure of formulants is not required. Information regarding the identity and quantity of formulants in pest control products is considered confidential business information and is protected from disclosure. However, any formulants which have been identified on EPA List 1 Inerts of Toxicological Concern are disclosed on the product label using the following statement: "This product contains x percent of the ingredient y which has been identified as having toxicological concerns." This disclosure is a policy and is not part of the legislation. In addition, PMRA has moved away from the use of the term "inert" or "non-toxic" ingredient in describing the non- active ingredients of a formulation as many of these may be inherently toxic.

Other issues

162. Acute toxicity testing on a mixture may give an initial indicator of possible antagonism or synergism from the combination of the ingredients.

163. There are no special considerations for mixtures that separate.

European Union

164. The legislative system of the European Community for pesticides consists of two different pieces of legislation. Firstly, provisions on the classification, packaging and labelling and secondly provisions on authorisation of pesticides for the market.

165. Specific provisions concerning placing of plant protection products (agricultural pesticides) and biocides (domestic pesticides, disinfectants, wood preservatives etc.) on the market set conditions and requirements for authorisation. They specify also testing requirements for authorisation purposes.

166. The present provisions for classification and labelling of pesticides are outdated in the European Community as they cover only a few dangerous properties. The new Directive on classification and labelling of dangerous preparations will include also pesticides in the scope allowing all dangerous properties to be taken into consideration in the classification. Biocides (domestic pesticides, disinfectants, wood preservatives etc.)are covered by the general provisions for classification and labelling.

167. Competent authorities apply the provisions for classification when specifying the classification and labelling for a plant protection product or a biocide for the authorisation. The conventional method for classification is applicable. If the pesticides are tested for authorisation purposes then they will be classified on the basis of test results.

United States

168. US EPA: In the United States, the Federal Fungicide, Insecticide and Rodenticide Act (FIFRA) provides for classification of all pesticides with attendant labelling. The Act gives the Office of Pesticides Programs in the US the authority to regulate pesticides for any health or environmental endpoint. This includes labelling, data collection, establishment of criteria for endpoint categorisation and labelling, or establishing restrictions on use. Regulations have been promulgated which specify that all pesticides be labelled for acute toxicity (oral, inhalation, dermal), skin irritation, eye irritation, sensitisation, and toxicity to fish and wildlife and pollinating insects. In addition, pesticides have been labelled for carcinogenicity and reproductive effects. Each pesticide product is labelled for its own individual hazards as determined from data submitted for registration. Pesticides are classified and labelled for all conditions of use be they normal use, accidents, misuse, etc. System assumes a wide range of scenarios from workplace to residential use. Classification under FIFRA has consequences in addiction to hazard communication such as restricting use to certified applicators for highly toxic pesticides. Many risk management practices can be used. For example, application may be allowed only in closed cabs. Hazard assessment is done by skilled scientific experts in the pesticide program who evaluate toxicological data on pesticide active ingredients and products. Standard Evaluation Procedures have been issued for this assessment. OSHA has the authority to require MSDS's for pesticides. However, the severity of labelling language and symbols required under FIFRA affects the choice of products purchased in the marketplace. Pesticide producers often reformulate to achieve less severe warning language and symbols. In those cases, bridging logic may be applicable to reduce retesting.

Definition of substance/chemical, mixture/preparation

169. The statute, under sec. 2(a), defines pesticides, active ingredients and inerts. Most pesticide products are preparations or mixtures. Products consist of at least one active ingredient and one or more inert ingredients.

170. Under the regulations in 40CFR Part 152.3, Active Ingredient means any substance (or group of structurally similar substances if specified by the Agency) that will prevent, destroy, repel or mitigate any pest, or that functions as a plant regulator, desiccant, or defoliant within the meaning of FIFRA sec. 2(a). The technical grade of the active ingredient is the active chemical as it is produced in the factory.

171. Inert Ingredient means any substance (or group) other than an active ingredient, which is intentionally included in a pesticide product.

172. Pesticide Product means a pesticide in the particular form (including composition, packaging, and labelling) in which the pesticide is, or is intended to be, distributed or sold. The term includes any physical apparatus used to deliver or apply the pesticide if distributed or sold with the pesticide. Pesticide products can be manufacturing use products or end use products. End use products consist of the technical grade of the active ingredient and all inerts in the formulation as it is intended to be applied for pest mitigation. Manufacturing use products are products other than end use products and consist of the technical grade of the active ingredient and stabilisers or solvents.

Classification of pesticides

173. The Office of Pesticide Programs, using data and information provided by pesticide registrants classifies all pesticide products. Pesticide products can be end use products, manufacturing use products, or the technical grade of the active ingredient if the technical pesticide is a manufacturing use pesticide. (See the appendix for definitions.)

174. Applicants for pesticide registrations submit health and safety data. The Agency has promulgated regulations under 40 CFR Part 158 that describe the data required for registration.

175. Studies for acute hazards are performed on the active ingredient and each formulated product. Studies for chronic health hazards are performed on the active ingredient. Studies for aquatic hazards are performed on the active ingredient and typical products; products that are substantially similar to typical products may not require testing.

Classification for environmental hazards

176. Labelling for aquatic hazards of pesticide products is based on data for the active ingredient only. At 40 CFR.Part 156.10(h)(2)(B), regulations require that "If a pesticide intended for outdoor use contains an active ingredient with a fish acute LC_{50} of 1 ppm or less, the statement "This pesticide is Toxic to Fish" is required for the pesticide product.

Classification for acute health hazards

177. The pesticide registrant has the obligation to test each active ingredient and all pesticide products for all acute human hazard endpoints subject to hazard labelling. Pesticide products are classified for acute toxicity by the oral, dermal and inhalation routes and for skin and eye irritation and sensitisation. The regulations at 40 cfr Part 156.10 require that all pesticide products be labelled if they fall into one of 4

hazard categories for acute toxicity, sensitisation, or irritation. The Agency has a policy of accepting bridging data to characterise substantially similar products for acute human hazard.

178. Pesticides are generally biocidal in nature and classification and labelling are intended to be protective to workers and bystanders. Bridging provides a way of using existing experimental data to characterise new products, amplified only by the addition of such data that are necessary to elucidate differences among products, while conserving resources and eliminating unnecessary animal testing. Inherent in the Agency's bridging policy are incentives for registrants to reformulate for safer products in that not all endpoints always need retesting.

179. If the Agency determines that a product (pesticide active ingredient and at least one inert ingredient) is substantially similar to a registered product, experimental data may not be needed to characterise all or any of the acute hazards of the similar product. The Agency's policy and the decision logic for use of bridging data is described below.

Case A: If a product is experimentally characterised for acute toxicity, irritation and sensitisation, and an inert ingredient is changed, additional testing may not be needed if the Agency determines that the new inert is of equivalent toxicity to the original inert. However, if the new inert has the potential to be of different toxicity in one of the six acute hazards, for example skin irritation, the new product can be accepted for registration upon submission of test data for that area (skin irritation in this example). When the new and original inert ingredients are both of moderate toxicity, the Agency may use published data and information on toxicity to determine their relative toxicities. In some cases, an inert of moderate toxicity is replaced with an inert which is totally nontoxic. Such inerts are comprised of fillers such as corncob grits or foods such as vegetable oil or cookie crumbs. Nontoxic inerts are on the Agency's List D and are typically classified as Generally Recognised as Safe (GRAS) by the Food and Drug Administration.

For example, registrants may wish to reformulate a product to remove precautionary statements about eye irritation. To that end, they may replace a surfactant (surfactants are often irritants) with a non-irritating inert such as vegetable oil. The new formulation would be tested only for eye irritation and the new toxicity category would be applied to it for that hazard, i.e. the data bridged from currently registered products would cover the new formulation; in essence the data is cited or waived. The formulation would not be required to be tested for the other acute endpoints, but rather the original classifications would apply.

Case B: If two ingredients are used in two different ratios in two pesticide formulations and data are available for toxicity of both products and both products fall within the same toxicity category, the Agency can interpolate for toxicities of products with intermediate concentrations of the two ingredients without requiring additional testing.

Case C: When a product contains more water than a registered product that is fully characterised as to its toxicity, the Agency will adjust the lethality value according to the dilution factor and assign a classification based on the adjusted lethality. However, in the absence of testing, the new

product will be assigned to the irritation and sensitisation toxicology category of the original more concentrated product. Generally, this case also applies to reformulation using nontoxic (List D) inerts.

Case D: If a registered product which is in the highest toxicity category (category I) is reformulated by removing water or other non-toxic ingredients, the new formulation is also assigned to toxicity category I. If the original product is not in the highest toxicity category for lethality and it is reformulated by removing some or all of its non-toxic ingredients, and if information is provided to show that the mechanism of toxicity of the toxic ingredients is not to be subject to enhancement by concentration, then a new toxicity category may be assigned by adjusting the formulation's lethality values according to the change in concentration.

180. An example of a situation when concentration factors would not allow the original data to be bridged is as follows. Products which are corrosive could gain faster entry into the body when more concentrated. In those cases, the toxicity could be enhanced when the product is concentrated.

181. Sensitization: If a pesticide product is characterised as a sensitiser, the classification for this endpoint will not be changed if the product is reformulated to change the concentration, but not remove, the sensitiser.

182. Other considerations: A product or active ingredient with a pH of less than 2 or greater than 11.5 need not be tested for skin or eye irritation, but will be assigned to the highest class for irritation. A product or active ingredient which is corrosive to the skin need not be tested for eye irritation, but will be assigned to the highest classification for eye irritation.

CONSUMER PRODUCTS

183. A comparison of the major classification systems for consumer products is given in Appendix II Table IV-5. In the USA, classification of consumer product is not restricted to hazard, but is based on the likelihood of injury, which accounts for dose-response and exposure. The consumer product regulations in the USA do not cover consumer pesticides, food nor pharmaceuticals. The EU system for classification of consumer products, with some exceptions, is the same as the EU workplace system. In Canada and the USA the manufacturer, importer or distributor is responsible for the classification; testing is not required; and there is flexibility where there is incomplete data. Canada does have a standardised approach for consumer product mixtures, as does the EU. In the USA, there is not a standardised approach for the classification of consumer products.

Canada

184. The criteria apply only to components or generated products to which the user or others might become exposed in normal use or reasonably foreseeable use. The Regulations do not apply to a consumer chemical product if a user cannot be exposed to the product or to any of its hazardous ingredients during normal use or reasonably foreseeable use.

185. For consumer chemical products the following steps are used in the process of test data interpreted/used:

- Human experience data take precedence over data from animal experimentation in categorising products. Human experience data means data demonstrating that an injury to a

person or a reversible or irreversible material impairment to the health or functional capacity of a person could result from a) exposure to a consumer chemical products; or the foreseeable use of a consumer chemical product or container by a consumer, in particular, the consumption of the product by a child.

- LD_{50} and LC_{50} values from tests conducted according to the OECD Test Guidelines for acute toxicity testing have been adopted as the core of the criteria scheme.

- When tests on animals are not appropriate or have not been conducted in accordance with the OECD Test Guidelines, results of other acute toxicity tests of the product or of its ingredients, conducted in accordance with a) a national standard or a recognised international standard, or b) a generally accepted procedure that accorded with good scientific practices at the time the tests were conducted are accepted.

186. If the product is a mixture, the LD_{50} and LC_{50} of each ingredient in the product that is present at a concentration of 1% or more, are determined using the additivity formula.

187. Results of tests conducted on or with a product, material or substance that has similar properties, in a) a national standard or a recognised international standard or b) a generally accepted procedure that accorded with good scientific practices at the time the tests were conducted, or c) other current information about the product that is known to the scientific community are accepted.

188. The use of professional judgement takes precedence over the use of a mathematical formula in estimating the toxicity hazard. Under the umbrella of professional judgement, it would be necessary to examine the human data - where it comes from and to what end-point it is being applied. For example, some epidemiological studies for chronic end-points may be biased or the human sample size too small to be acceptable, whereas, a well-conducted study for skin irritation on 1000 humans would be acceptable. There will always be different opinions or judgements on what is considered reliable data. The task of determining what data is reliable is the challenge or reality we must accept.

189. For consumer systems, the use of bridging data is not specifically required, however, may be covered under the umbrella of professional judgement.

190. If the mixture as a whole is not tested, then provisions exist for estimating the toxicity of the mixture based on the toxicity of the individual components e.g., the additivity formula.

191. If the LD_{50} or LC_{50} of one or more ingredients present in the toxic product in a concentration of 1% or more is not known, the person responsible may use an estimated LD_{50} or LC_{50} determined in accordance with good scientific practices. Where the LD_{50} or LC_{50} is unknown and cannot be estimated, the LD_{50} or LC_{50} of the untested component be equal to the LD_{50} or LC_{50} of the most toxic known component present at over 1% w/w. (Note: This value is then used in the additivity formula to determine the LD_{50} or LC_{50} for the mixture). A cut-off is needed when using the additivity formulas because many products contain large numbers of trace components which, while not significantly affecting the toxicity, would render use of the additivity formulas prohibitively complex. The specific cut-off value, 1% w/w, is the same as that specified in the *Controlled Products Regulations* (WHMIS).

192. A list of substances of special concern have been developed for substances which are known to be toxic through human experience, test results or professional judgement, each substance is classified differently according to whatever the concentration of the toxic component is found in a mixture. For example, products containing ethylene glycol are classified as toxic when found in solutions greater than or

equal to 5% w/w, where if found in concentrations less than 5% w/w but greater than or equal to 2% w/w are classified as harmful. There are 10 substances of special concern for consumer chemicals. These substances are of special concern because standard animal tests may not reflect the actual hazard posed by them to humans.

193. Some criteria e.g., flammability are based on physical state, while other e.g., toxicity are divided based on route of exposure. For the inhalation route of exposure, gases, vapours and dusts/mists have different criteria.

194. Components of consumer chemical products may separate out over time, especially in the case of emulsions of petroleum distillates. Estimation of the toxicity of the product as a whole in such cases may significantly misrepresent the hazard when the upper supernatant layer will be accessible as a distinct mixture or solution and may be so ingested by a child. Therefore, in the case of a supernatant mixture, the toxic product must be assigned the LD_{50} or LC_{50} value of the most toxic layer.

195. No consideration for impurities/contaminants less than 1% (w/w), however, if the supplier is aware that this impurity constitutes a hazard, then professional judgement would take precedence, whether the guidelines called for it or not.

196. No consideration for synergistic and antagonistic effects. There have been few systematic studies of toxicological interactions among the chemicals commonly present in consumer products. One large study of interactions determined the oral LD_{50}'s of all possible combinations of 27 industrial chemicals, including carbon tetrachloride, ethanol, ethylene glycol and toluene. The ratios of measured to predicted LD_{50}'s (predicted using the additivity formula) were mostly very close to 1, with some random variation above and below. Other studies have shown similar results. Thus the available information indicates that the acute toxicity of mixtures of such chemicals is reasonably well predicted by the additivity formulas.

197. Equivalent formulas have been adopted by regulatory agencies for calculating the occupational exposure limits of mixtures of hazardous substances in air. For example, the American Conference of Governmental Industrial Hygienists (ACGIH), which develops the Threshold Limit Values (TLVs), advises that "in the absence of information to the contrary, the effects of the different hazards should be considered as additive."

198. There are no specific criteria for mixtures that would not require new evaluations when concentrations of initial ingredients are changed or new components that have very similar or the same properties are substituted. If the product is changed, then there would be a need to reclassify to ensure that the labelling does not change too, particularly where classification would be increased.

199. Exposure (risk) and seriousness of effect are taken into consideration for consumer products. This is dealt with through the warning labels. For classification criteria, potency has not specifically been dealt with at this point since potency, which mainly applies to chronic end- points, have not yet been developed for consumer products.

200. Risk of exposure is considered by consumer products. For example, if components are inaccessible to the user during normal use or reasonably foreseeable use, then they are not subject to the criteria.

201. Classification also determines which products will require pre-market review (permission prior to sale) and which products will require child-resistant containers.

202. In addition to labelling, the *Consumer Chemicals and Containers Regulations* requires certain products (determined by classification) be packaged in child-resistant containers to reduce the likelihood of injury and illness should a child come in contact with a product. No specific regulatory requirements exist for training or other exposure control systems. A consumer education and information program has been established, however, this does not compare to the training received by workers. In additions, engineering controls and personal protective equipment are not necessarily present in homes.

European Union

203. For consumer products the general scheme of the EU directive of preparations is followed for their hazard classification in order to make it possible to apply a hazard warning. The manufacturer has the responsibility that no health damaging products may be put into the market by applying a full risk evaluation.

204. For some categories of consumer products a full risk evaluation is done as foreseen by Community Directives and consequently a more risk based warning system is applied. These categories are therefore exempted from the substances and preparations directives. The following preparations in the finished state, intended for the user are exempted: medicinal products for human or veterinary use, cosmetic products, mixtures in the form of waste, foodstuffs, animal feeding stuffs, radioactive substances, other substances or preparations for which Community notification or approval procedures exist and for which requirements are equivalent to the substances directive 67/548/EC.

US: FHSA

205. In the USA, consumer products are generally regulated under the requirements of the *Federal Hazardous Substances Act* (FHSA). There are exceptions, however, including consumer product pesticides, food, drugs and cosmetics, all of which are addressed under the requirements of other agencies. The Consumer Product Safety Commission (CPSC) is responsible for implementing the FHSA requirements. As noted in Table IV-5, the primary objective of CPSC's regulations is to determine the likelihood of injury or illness posed by the product**.**

206. In order to accomplish this, the manufacturer, importer or distributor of a product must evaluate all available information to ascertain what the potential hazards of the product may be. This would be based on test data where available, but testing is not obligatory. The assessors may also use published data, past experience on similar products, human experience or an expert opinion. The assessment may be based on the chemical composition in some situations; SAR; extrapolation; or estimation. While there is no standardised approach using percentage cut-offs or concentration limits, formulae from the scientific literature may be used to predict the hazard when data permit. Evaluations based on extrapolation or estimation would be considered under the category of bridging data.

207. CPSC's regulations may result in a label on the product. The Agency considers the process of "classification" to include both the identification of the hazard and an assessment of the likelihood of harm to the user under normal conditions of use or foreseeable misuse. Criteria for classification and labelling for acute hazards and physical effect were derived as values that posed likelihood of injury from a single exposure and thus do not require further assessment of likelihood of injury, the Agency however require an assessment of likelihood of injury or illness to be performed when determining whether a chronic hazard is to be placed on the label. The evaluator may take into consideration the dose or exposure expected when the product is used by consumers in determining whether the hazard needs to be included on the label. The underlying assumption to this approach is that consumer exposure is often brief and intermittent, and,

unlike worker exposure situations, not of a nature to lead to the development of a chronic health effect. While this is an issue that will ultimately be addressed under the work of the ILO on hazard communication, it is a basic difference in approach from the other systems' consumer products requirements that should be factored into the discussions in this area. Additional technical factors regarding the US CPSC mixtures approach in response to the questions posed:

- CPSC considers substantial personal injury or substantial illness as a result of any customary or reasonably foreseeable handling or use, including reasonably foreseeable ingestion by children. Susceptible population groups such as children or the elderly are given special consideration in the determination of likelihood of injury or illness for their increased susceptibility and special exposure conditions and other similar factors.

- If the toxicity of the components is unknown the mixture is tested. Since our system is based on the likelihood of adverse effects, if a component is not available or accessible for exposure, its contribution may not be taken into consideration. However, when a mixture is tested the values obtained are used for classification, even if the component did or did not contribute to the toxicity.

- The mixture is thoroughly mixed before test is conducted. Special consideration is not given unless there is clear impact on potential for adverse effects. Impurities and contaminants are treated in the same manner as other components.

- When the toxicity of a mixture is determined by extrapolation from toxicity of components and the synergistic or antagonistic effects of ingredients is clearly established, such an effect may be taken into account. Expert judgement that takes into account the toxicity of the components that have changed and the change in concentration provide guidance when the formulation of a mixture changes.

- With regard to bridging data, CPSC allows the use of test data, toxicity values extrapolated from the toxicity of components, human data including experience and expert opinion based on available valid and acceptable data. Extrapolation is similar to the bridging used by EPA. Valid and acceptable human data including experience take precedence over other data.

- All relevant factors that may impact the likelihood of injury or illness from the use of a mixture are considered during the classification process. These include exposure, potency, and others.

- Classification system in itself is not used for purposes other than labelling. However, generally classification is first step in evaluation of adverse impact on health. In addition or in lieu of labelling, other appropriate regulatory steps may be taken to reduce or eliminate the adverse health impact. In order to reduce or eliminate adverse health impact from a substance or mixture, in addition to appropriate regulatory action (including labelling but independent of labelling), CPSC may prepare educational material for public distribution, or may provide public service announcements on radio and television.

COSMETICS

208. A comparison of the major classification systems for cosmetics is given in Appendix II Table IV-6. Regulation of cosmetics in Canada, the EU and the USA does not include hazard classification for cosmetics at the point of consumer use. Classification criteria will not be developed for these cosmetic mixtures. However, cosmetic mixtures are covered in some workplace systems and these product mixtures will be further considered in the classification criteria proposal. There is no standardised approach to mixtures.

ENVIRONMENTAL HAZARDS

209. The existing procedures for determining the environmental hazard of mixtures are less well-defined than the procedures for determining the hazard for human health. Appendix V presents the criteria used in the EU system based on measured or calculated toxicity.

210. It should be noted that a systematic approach to the classification of the environmental hazards for mixtures has been proposed in the EU system. Some systems use only a single aquatic toxicity cut-point to define the hazard of a mixture. For some systems, where a mixture contains a chemical with a known toxicity, the hazard of a mixture is determined by a concentration cut-off point. Moreover such cut-offs may vary (i.e., chemical specific).

211. The new GHS classification system for hazardous for the environment, which was recently approved at the OECD, depends on combinations of three levels of acute toxicity, ready biodegradation and potential for bioaccumulation. The system provides for three levels of environmental hazard. A Guidance Document concerning data interpretation and application in the classification system. This guidance will have important implications for classifying both dilute solutions of one hazardous chemical and mixtures of two or more hazardous chemicals.

212. The UNRTDG and the Canadian TDG Regulations are expected to be changed, and the EU criteria and procedures have been amended but not yet formally adopted.

United States

Regulations under *Federal Insecticide, Fungicide and Rodenticide Act*

213. Labelling for aquatic hazards of pesticide products is based on data for the active ingredient only. Regulations require that “if a pesticide intended for outdoor use contains an active ingredient with a fish acute LC_{50} of 1ppm or less, the statement: “This pesticide is toxic to fish” is required for the pesticide product regardless of the concentration of the active ingredient. It the other components of the pesticide formulation are toxic or may affect the toxicity, i.e., by enhancing the uptake of the active ingredient, the formulation is to be tested and the lowest toxicity is used for classification.

Canada

Transport

214. The current Canadian Transport of Dangerous Goods Regulations treat Class 9 somewhat differently than the UNRTDG. The Class has three Divisions: 9.1 Miscellaneous dangerous goods; 9.2

Hazardous to the environment; and 9.3 Dangerous Wastes. Divisions 9.2 and 9.3 would be applicable to mixtures.

215. All classifications of 9.2 have been assigned by the competent authority. Where a subsidiary classification of 9.2 has been assigned, that classification becomes primary in a mixture only when the cut-point of the original classification (acute toxicity, corrosivity, flammability, etc.) has been surpassed. Cut-points for environmentally hazardous substances beyond which transport regulations no longer apply are substance specific and are measured in kg of substance per package.

Pesticides

216. The Pest Management Regulatory Agency does not have an environmental hazard classification *per se* for pest control products. Testing for acute toxicity to fish, aquatic and terrestrial inverta, plants and birds is required for each active ingredient and the lowest NOEC, NOEL or EC's for plants is used directly in a risk assessment related to the planned or expected use of the product. These assessments are used to establish conditions for safe use, e.g., buffer zones, which are included on the label.

217. PMRA is proposing to use various environmental criteria (including toxicity to fish and birds, bioaccumulation potential and a leaching index) as criteria for the establishment of restricted, commercial and domestic control product categories. These criteria would supplement the existing toxicity (i.e., acute mammalian LD_{50} criteria).

HAZARDOUS WASTES

218. While the charge for the development of the GHS is contained in Chapter 19 of Agenda 21 of the UNCED Agreements, which relates to the environmentally sound management of toxic chemicals, hazardous wastes are dealt with in Chapters 20 (management of hazardous waste), 21 (management of solid waste and sewage-related issues), and 22 (management of radioactive wastes).

219. Questions relating to the management of hazardous wastes internationally are already the subject of extensive efforts under the Basel Convention, on the Management of Hazardous Wastes. The Annexes to the Basel Convention include definitions of hazardous wastes and lists of wastes and waste streams within various hazard classes. Under the Basel convention, "wastes" are generally defined as substances or objects which are disposed of or are intended to be disposed of or are required to be disposed of by the provisions of national law. The hazardous characteristics covered by the convention include: explosive, flammable liquids, flammable solids, substances or wastes liable to spontaneous combustion, substances or wastes which, in contact with water emit flammable gases, oxidising, organic peroxides, poisonous (acute), infectious substances, corrosives, liberation of toxic gases in contact with air or water, toxic (delayed or chronic), ecotoxic, capable, by any means, after disposal, of yielding another material, e.g., leachate, which possesses any of the characteristics listed above.

220. Generally, hazardous wastes are classified in the same way as dangerous goods are in the UN Regulations on the Transportation of Dangerous Goods (UNRTDG). Hazardous wastes are those dangerous goods:

- that are no longer used for their original purpose, and
- that are intended for treatment and/or disposal, or
- that are recyclable materials.

221. Hazardous wastes are included under UNRTDG Class 9 - Miscellaneous dangerous goods. This class has a sub-class 9.3 for hazardous wastes. Sub-class 9.3 currently is being implemented by individual UN countries on the basis of lists of waste types and leachable toxic waste. Examples are the EU Seveso Directive and the Canadian Export and Import of Hazardous Waste Regulations. The relevant Annexes to the Basel Convention are being revised in order to refine, upgrade, and quantify the international approach used for classifying hazardous wastes.

222. In view of these activities within the hazardous waste sector, no summaries have been included in the Appendix to the document.

223. The answers by the major systems to the additional question on hazardous wastes from the questionnaire are given below.

Canada

224. Hazardous wastes are presently exempt from workplace (WHMIS) classification. They are classified only if they have to be transported and are classified and labelled according to the Transport of Dangerous Goods Regulations.

European Union

225. Directive 75/442/EEC on waste with a modification of Directive 91/156/EEC introduces a definition for waste:

> "any substance or object contained in Annex I (note that this is irrelevant because of entry 16 of Annex I of directive 91/156/EEC) which the holder discards, or is obliged to discard or has the intention to discard".

226. Directive 91/689/EEC on hazardous waste defines the term ‘hazardous waste’ by introducing lists of product types (Annexes I and II) which may be considered to be hazardous within the scope of the Directive. The waste may be in liquid, sludge or solid form.

227. The hazardous waste specified in Annexes I or II must have one or more of the properties listed in Annex III. The origin and composition of the waste and, when necessary, limit values of concentration have to be taken into consideration. All wastes fulfilling the criteria specified for substances and preparations in Annex III may be considered as hazardous.

228. The properties of wastes which render them hazardous are:

H1	Explosive
H2	Oxidizing
H3-A	Highly flammable
H3-B	Flammable
H4	Irritant
H5	Harmful
H6	Toxic
H7	Carcinogenic
H8	Corrosive
H9	Infectious
H10	Teratogenic
H11	Mutagenic

H12	Substances and preparations which release toxic or very toxic gases in contact with water, air or an acid.
H13	Substances and preparations capable by any means, after disposal, or yielding another substance, e.g. a leachate, which possesses any of the characteristics listed above
H14	Ecotoxic

229. Attribution of the hazard properties toxic, very toxic, harmful, corrosive, irritant, carcinogenic, mutagenic and teratogenic is made on the basis of the criteria laid down by Annex VI of Directive 67/548/EEC.

230. The concentration/cut off limits for mixtures are laid down by a Council Decision 94/904/EC as follows for groups H3 to H8:

- flash point $\leq$ 55 °C
- very toxic $\geq$ 0.1% (total concentration)
- toxic $\geq$ 3 % (total concentration)
- harmful $\geq$ 25 % (total concentration)
- corrosive (R35) $\geq$ 1% (total concentration)
- corrosive (R34) $\geq$ 5 % (total concentration)
- irritant (severe eye irritation, R41) $\geq$ 10 % (total concentration)
- irritant (eye, skin or respiratory irritation, R36, R37, R38) $\geq$ 20 % (total concentration)
- carcinogenic cat. 1 or 2 $\geq$ 0.1 % (total concentration)

231. These concentration limits correspond to the classification of dangerous preparations.

US

232. Hazardous wastes are regulated, classified and labelled under the Resource Conservation and Recovery Act (RCRA). RCRA's main goals are to protect human health and the environment from the potential hazards of waste disposal and recycling, to conserve energy and natural resources, to reduce the amount of waste generated, and to ensure that wastes are managed in an environmentally sound manner. Specifically, RCRA Subtitle C establishes a framework for managing hazardous wastes from generation until ultimate disposal. Hazardous wastes can be solids, liquids, gases or sludges that are either specifically listed on one of four lists ("f" hazardous wastes from non-specific sources; "k" hazardous wastes from specific sources; "p" acutely hazardous discarded commercial chemical products; and "u" toxic discarded commercial chemical products) or that exhibit at least one of four characteristics of hazardous waste: ignitability, corrosivity, reactivity; and toxicity.

233. The OSHA Hazard Communication Standard includes specific exemptions for hazardous waste as follows:

> Any hazardous waste as such term is defined by the Solid Waste Disposal Act, as amended by the Resource Conservation and Recovery Act of 1976, as amended (42 U.S.C. et seq.), when subject to regulations issued under the Environmental Protection Agency.
>
> Any hazardous substance as such term is defined by the Comprehensive Environmental Response, Compensation and Liability Act (CERCLA) (42 U.S.C. et seq.) when the hazardous substance is the focus of remedial or removal action being

conducted under CERCLA in accordance with Environmental Protection Agency regulations.

VI. ANALYSIS OF SIMILARITIES AND DIFFERENCES

234. Scope: In Canada the classification of chemicals in consumer products and workplace chemicals are covered by different pieces of legislation. For the workplace physico-chemical properties and toxicological properties of the preparation are taken into account. For consumer products physico-chemical properties and only acute toxicogical hazards are taken into account. In the EU the classification of preparations is covered by a single piece of legislation, that can be applied across all product types and use categories defining clearly all end-points which need to be considered. Physico-chemical, toxicological and environmental properties are included. In the US chemicals in the workplace and in consumer products are covered by different pieces of legislation. Physico-chemical and toxicological properties are considered. Transport is covered by UN MRTDG in which physico-chemical properties and acute and corrosive effects are taken into account. Classification of pesticides is covered by separate legislation in Canada and the US, whereas in the EU it is proposed to be covered by the general legislation for preparations.

235. Exclusions/Exemptions: In Canada the exclusion of certain products under workplace regulations is under review. In the US similar exemptions are used. In addition waste and consumer products in their final form such as food or alcoholic beverages, drugs, cosmetics are also exempted. The US work place regulation has a set of exemptions for which other laws and regulations apply, for example, as in Canada, wood or wood products, manufactured articles, tobacco and tobacco products as well as medical/veterinary devices. In the EU similar exemptions apply to such products, which are governed by specific legislation. This extends in the EU also to medical devices.

236. Rationale: In the US, EU and Canada mixtures are classified for their hazards. Subsequently it is used to provide the information to workers, employers and consumers. In addition the classification is used in the EU for other purposes like restrictions for marketing and use to protect man and environment. In the US and Canada, some sectors (consumer products and pesticides) consider some elements of risk (exposure) to determine labelling requirements. The UNCETDG has a pragmatic approach to mixtures, which intends to allow the consignor to identify (without unnecessary difficulties or costs) the hazard characteristics of the mixture. Additional downstream consequences like prohibition/permission for transport and permitted packaging types and sizes can be expected.

237. For animal welfare reasons and available principles it is advocated in the EU, in cases when there are no requirements for testing, to use the standard approach for untested mixtures. Testing in order to assess the CMR hazards of mixtures is not allowed in the EU because of insufficient reliability of results.

238. Comparison of systems: The evaluation of reliable data for the mixture/preparation is used by all systems in order to classify the mixture/preparation. When one individual substance of the tested mixture/preparation is changed for another individual substance (for which the toxicity is known), all systems allow extrapolation of the test result. In the US, a standardised approach is only used for workplace chemicals. In Canada, a standardised approach is used for workplace and consumer chemicals. In the EU all kinds of preparations may be classified using the standardised approach. In the transport system a standardised approach may be used for acute toxicity.

239. When used for information purposes comparable general concentration limits in the range of 0.1% to 1% are used for safety data sheets in all systems.

240. The EU classification system allows for the determination of acute toxicity and corrosion/irritation of the non tested preparation the application of the dilution principle (extrapolation to lower hazards classes for these endpoints) in order to approach the comparable results obtained by testing.

241. For acute toxicity additivity rules are applied using a combination of all routes of exposure (EU) or one route only (Canada and the transport system).

242. In the EU a more severe general concentration limit is used for the highest hazard CMR classes than for the lowest hazard CMR class as compared to the US and Canada who have only one concentration cut-off.

243. For consumer products only acute health hazards are evaluated for hazard classification in Canada. In the US both acute and chronic health hazards are subjected to risk evaluation and a subsequent reduction in hazard labelling. In the EU however the consumer products are subject to the same classification procedures as for all other preparations placed on the market.

244. Where a specific concentration limit has been set for a substance this must be used in stead of the general limits in the standardised approach (EU). In the case of exceeding exposure levels in the workplace a hazard classification is also possible when a concentration less than the cut-off values is present for a certain component in a mixture (US).

245. The Expert Group on Classification Criteria for Mixtures held a one day workshop to illustrate conceptual, technical and practical differences between and existing systems and more importantly, to identify commonalties. A summary report of the Workshop will be provided separately.